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PREVENTION OF INJURIES IN COLLEGE ATHLETICS

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The records of 14,375 contestants in organized college athletics over a period of 17 years, embracing 36,050,885 practice-periods or games, showed 3,453 injuries severe enough to exclude the player from one or more subsequent practice or game sessions. This high incidence of 24% indicates the need for insisting on the player's "bill of rights" which is here stated. It includes good coaching, good equipment, and good medical care. The medical care includes a thorough preseason examination, the presence of a physician on the playing field, and due respect for his authority. A case history illustrates the prolonged disability and permanent residual damage done by ill-advised treatment of athletic injuries. Responsibility for diagnosis and treatment of athletic injuries should not be imposed on coaches and trainers but assumed and duly discharged by the physician.

THERE APPEARS to be general agreement that the incidence of injury in the United States is too high. Industry has reduced the incidence of industrial accidents markedly by a continuing educational and training program among its plant supervisors. Highway safety engineers have so far been unsuccessful in reducing the accident and death rate among our motoring public. The true incidence of sports injuries is not known for lack of accurate statistical data. Were this incidence known, something would be done about making our athletes, our coaches, trainers, and team physicians, the sports rules committees, and the sports equipment manufacturers more conscious of their responsibility in providing more safety measures. Our experience with the incidence of sports injuries is presented in table 1.[1]

In a period of 22 years this demonstrates the great increase in sports participation at our college. Considering that the intramural program this winter included 52 hockey games, 113 basketball games, and 152 squash racquet team matches, one realizes that student participation in exercise activities is high. In all sports this program averages 2,400 individual students, more than 50% of college enrollment. In varsity, junior varsity, and freshman sports, an estimated additional 1,700 of the college enrollment should be included. In other words, about 76% of our college student body is participating in organized sports.

In table 2 an attempt has been made to analyze the incidence of injury in 17 academic years (fall of 1936 through spring of 1954) by the number of exposures (practice or game sessions). I am not cer-

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tain just what one can derive from this computation. In recording injuries, only those injuries are recorded that prevent a player from participating in one or more practice or game sessions. However, 3,453 injuries among 14,375 contestants represents a high incidence, namely 24%.

TABLE 1.—*Total Number of Athletes in Organized Sports in Harvard College from Fall, 1932, to Spring, 1954*

Season	1932-1937	1937-1942	1942-1947	1947-1954*	Totals
Fall	3,271	2,477	703	6,485	12,936
Winter†	1,235	1,662	280	8,895	12,072
Spring	2,112	2,720	445	7,670	12,947
Total	6,618	6,859	1,428	23,050	37,955

*The last period is for seven academic years rather than five. Since 1947-1948 the varsity and junior varsity football participants have been averaged.
†The figures for winter sports include only hockey and winter track, the only major sports in that season until 1937, when swimming and basketball were made major sports.

Any program for prevention starts with the individual player, who is entitled to his "Bill of Rights." [2] These are as follows:

(1) Good Coaching. This has practically been realized. The coach who teaches unsportsmanlike tactics to win at any price is almost extinct. Almost all coaches today are competent instructors in the technical aspects of the game, ignorance of which greatly increases the incidence and severity of injuries.

(2) Good Equipment. This, too, can easily be achieved. The equipment manufacturers take their responsibilities very seriously and are continually modifying and improving the various types of armor worn in contact sport. The problem lies in the false economy of using worn out, outmoded, or ill-fitting gear. The outfitting of a team is no place for penny pinching.

(3) Good Medical Care—which has three aspects:

First—a thorough preseason history and physical examination. This is the most important single factor in the prevention of injuries. A considerable number of the tragedies which occur every year are due to medical conditions such as heart disease, hypertension, and diabetes which were not recognized and usually constitute contraindications to participation in contact sport. For many years at Harvard, loss of function of any of one paired set of organs has also been regarded as contraindication for participation in body contact sports. This rule produces an annual crop of unhappy young men who seem to have played for years in high school with one testis, kidney, or eye, but we have made no exceptions. Other less potentially dangerous sports are available, and no game is worth the risk of blindness, death, or castration.

Another important aspect of the preseason examination, particularly in high schools and preparatory schools, is the proper matching of players. Boys grow at different rates. Some at 15 have mature and well-coordinated musculoskeletal systems. Others are small and soft, having barely entered the wondrous years of adolescence, and still others are large-boned, skinny, and uncoordinated, being in a period of rapid bone growth, with barely compensated nerves and muscles.

To mix these types on a team is to look for trouble. This is an area for cooperation between coach and doctor. Well-matched teams are much safer and much more fun for all concerned.

Second—A doctor should be present on the playing field at every scrimmage and game. To leave to a trainer or coach such decisions as whether an injured player should continue play or be removed, whether he should be carried or walk off the field is to gamble with the player's future with the cards stacked against him.

Third—A doctor's authority in matters medical should be absolute and unquestioned. This principle is the measure of a good coach. Almost all coaches today are happy to leave medical decisions to the medical profession. They have enough difficult decisions and problems as it is.

Granted that this "bill of rights" has been fulfilled, injuries will still occur. Fortunately the very great majority are minor, and fall into the category of contusions, strains, and sprains.

With this "bill of rights" understood by coach, trainer, doctor, and player, each must play his part in coordinating the measures required to minimize the injuries. In contact sports the teaching of special techniques and the timing in coordinated team play are factors often not understood by the casual observer. It requires long hours of practice to develop timing in a team, and this is practice in live scrimmage. The doctor and trainer must be trained to observe and detect a "limping" or a "groggy" player from some yards distance. Continued play on a minor sprained ankle can aggravate a grade 1 lesion and often may result in an unnecessarily prolonged disability period. Each day of disability is a day lost not only in the player's development but also in the squad or team development. From our experience recurrent sprains can be controlled by protective adhesive strapping daily, plus a progressive resistance exercise program to the muscles in and about that joint. This is essentially controlled under the direction of doctor and trainer for the benefit of the player.

Preseason conditioning exercise to develop muscle tone on schedule is absolutely necessary. Within the last few months Professor Emeritus McCloy of the State University of Iowa has prepared and published a program for the National Federation of High School Athletic Associations which has been distributed to the members of this association. The exercise program is clearly defined and illustrated and can be followed by each preseason candidate at home. This is a great step forward, and if carried out in our high schools and colleges should have a significant influence on the early season injury incidence. Not only sprains but muscle or tendon strains are the bugbear of coaches and doctors in early season practice. Such can be prevented by the players returning for the first session of practice preconditioned.

TABLE 2.—*Total Contestants and Total Injuries as Related to Total Exposures**

Sport	No. Out†	No. of Exposures‡	No. of Injuries
Fall	3,840	3,741,477	2,170
Winter	4,268	13,989,276	470
Spring	6,267	18,320,132	813
All	14,375	36,050,885	3,453

*Exclusive of intramural teams, fall, 1936-spring, 1954, inclusive; and excluding the years, fall, 1942-spring, 1946, for which complete figures are unavailable. Since 1947-1948 the varsity and junior varsity football figures have been averaged. Data from Thorndike,[1] p. 66.
†The figure in the "No. Out" column represents the average of men out in each sport each day.
‡An "exposure" is taken to mean one afternoon period of practice or play for each man in each sport.

Another item that contributes to injury incidence is the player's apathetic attitude toward proper adjustment of pads. It is not uncommon to find football players who neglect to tighten or lace their

shoulder pads or underarm elastic webbing straps. Furthermore, many of us have seen hip pads worn that are inadequate protection in order that the player in his own thinking might gain running speed. The proper wearing of protective equipment is the responsibility of coach, trainer, doctor, and player.

In the wide expanse of playing fields at Harvard, during the fall season, my staff consists of four surgeons and four trainers on the fields when contact sports are taking place. Through the week, one additional surgeon is in the field house clinic each afternoon and on Saturday one surgeon with each competing team other than with varsity football.

In order that the incidence of injury in organized athletics may be better known, it behooves those of us working with athletic trauma to report our results on a wide-scale basis. What is the true incidence in football, at the college level or at the high school level? Before one can determine such, one must have accurate records of diagnosis and period of disability of each injury on each college or high school squad, and until such a record is obtainable from the colleges and schools one hesitates to even hazard a guess. One fact is certain; namely, this incidence is too high, and the disability period in most instances is too long. From the coaches' point of view every day lost from practice not only hurts the player and his normal development in newly learned techniques but also hinders the whole squad's development.

In the past, several groups of interested associations have tried by questionnaires to obtain information on the incidence of injuries in sport, but the replies received were so few that the attempt at recording was abandoned. A recent study of this situation concerned all trauma on college campuses undertaken by the American College Health Association and the National Safety Council over a two-year period.[3] The first year 11 colleges participated, the second year 9. The report did not separate purely athletic trauma from other types, so that it failed to reveal anything on the incidence of trauma from sports. The National Federation of High School Athletic Associations is now embarking on a new attempt. One may rightly inquire as to where such a collection of data should be centered. To my mind, either the National Collegiate Athletic Association and the National Federation of High School Athletic Associations or the National Safety Council and the American College Health Association should be the source of such an annual report.

But can all colleges or schools render an accurate report of all athletic injuries? To obtain the complete picture of athletic trauma and its true incidence, it must cover all sports which are in intercollegiate and interscholastic competition. The records analyzed should be medical in origin and include at least an accurate medical diagnosis and the disability time lost from the squad season. With this material available from a good sample of schools and colleges, one can then draw significant conclusions. It can be undertaken regionally or nationally. Let us make a start toward accurately determining the true incidence of athletic trauma.

What measures can be taken to lessen the incidence of injury? Development of the rules of the sport, and the enforcement of these rules by the officials, is one item that has altered the incidence of injury. The protective equipment (padding) and its design is another. Just now we are looking for a better football helmet, and we think we have it, but the manufacturer can supply it in only one size. The design and construction of some pads afford little if any protection to the wearer. New materials are being tried in the fabrication of pads that have been inadequately tested in the laboratory and on the field. The third item, proved to reduce recurrent ligament sprains, is proper protective adhesive strapping for every practice or game. It matters significantly whether ligaments had been sprained in high school prior to entrance to college, and in such instances they receive daily strapping from the start of the season.

The purely medical prerogative is the diagnosis, treatment, and prognosis of all individual injuries once sustained. In addition, the prerogative pertaining to the prevention or aggravation of minor injury belongs to the medical staff. No one can deny that progress has been made in reducing the days of disability from athletic injuries. Table 3 demonstrates significantly the results of early, prompt treatment. Physicians, trainers, and coaches are all concerned with the individual player and his welfare. The permitting of a player with cerebral concussion to continue play should not be tolerated. Even the player who is exhausted physically and physiologically is more prone to injury if permitted to continue.

TABLE 3.—*Incidence of Sprains and Length of Disability Incurred in Sports at Harvard University*[a]

Sport	Ankle Sprains, No.		Disability Days		Knee Sprains, No.		Disability Days	
	1946-1947	1953-1954	1946-1947	1953-1954	1946-1947	1953-1954	1946-1947	1953-1954
Varsity football	7	2	55	35	4	5	34	46
Jr. varsity football	7	3	96	15	5	4	71	41
Intramural football	12	1	75	30	9	3	139	58
Totals	26	6	226	80	18	12	244	145
Av.			8.69	13.33			13.56	12.08

[a]From Thorndike, A.: J. A. M. A. **162**:1126 (Nov. 17) 1956.

A player not mentally or physically capable of carrying out his assignments is of less value to a team than a fresh substitute. Every follower of body-contact sports can recall having seen some player allowed to continue in a rugged contest without full capacity of his mental processes. In the high school leagues, particularly, there is lack of adequate medical supervision of practice sessions of contact sports. The responsibility lies in the community schools' committees.

According to Eastwood's report[4] of the nine football fatalities in 1955 that were a direct result of competition, six were deaths of high school play-

ers. It is unfair to a coach not to provide him with adequate medical assistance. Even though the majority of injuries sustained are not serious, nobody can prophesy when a serious accident might occur.

The team physician must grasp the opportunity to determine whether a limping player should be taken out of competition. He should arrange with the team captain to call time out for any needed examination. He should be familiar with the functional testing of joints, the more common sites of fracture, and the simpler tests for diagnosis of type of injury. In instances of head injury, he should be alert and ask the player simple questions in order to determine whether there is amnesia with loss of orientation of time and place. If necessary the physician could call on the team captain to interrogate the injured player in order to determine whether the player knew his particular assignment in an individual play signal. When an arm or leg is involved, comparative tests of the normal side and the injured side are simple and practical.

Once the injury is located and diagnosed, its severity or degree is the important decision to make. Will continued play turn a sprain from grade 1 into grade 2 or grade 3? In many instances one cannot determine the degree of injury until 24 hours later. The player should be protected from an unnecessarily long disability period. There is no reason, from a pathological point of view, to think that an acutely sprained ligament can be supported by adhesive strapping, so that the player can be returned immediately to play without doing irreparable harm to the injured ligament. The torn ligament must heal, and one cannot put stress on it until the healing process is complete, and then only with daily supportive adhesive strapping. It will never again be as strong, since there will be fibrous scarring. The too early return to play of a player with a healing sprained ligament can undo good results of the partial healing process. The team physician must determine when the lesion has healed and the player is ready to return to play. He must realize that, if a player still limps, an ankle sprain is incompletely healed and that, regardless of the amount of adhesive tape applied, the player cannot yet withstand the stress of running and dodging.

TABLE 4.—*Types of Injuries Incurred Most Commonly in Sports at Harvard University**

Injury	1932-1937	1937-1942	1942-1947†	1947-1952	1952-1954	Totals
Sprains	636	426	210	344	86	1,702
Strains	363	287	96	145	53	944
Contusions, joint	219	73	87	52	17	448
Contusions, muscle	526	350	111	60	18	1,065
Contusions, simple	281	93	103	97	22	596
Fractures and dislocations	223	232	105	181	47	788
Lacerations and abrasions	264	89	25	40	6	424
Inflammations and infections	300	131	66	48	9	554
Internal injuries	102	81	39	115	26	363
Miscellaneous	243	152	67	42	6	510
Totals	3,157	1,914	909	1,124	290	7,394

* Data from Thorndike,[1] p. 66.
† From fall, 1943, until spring, 1946, sports were on a wartime basis, with organized sports continued only informally and on a limited basis.

The team physician must become familiar with the more common types of injuries produced in athletics and likewise the more commonly injured parts of the body. Tables 4 and 5 illustrate my own experience. Alertness on the part of the trainer and team physician and recognition of the more serious and less common injuries is a "must" in organized sports. In most body-contact sports, there is a time limit of three minutes in which the one responsible for diagnosis and prognosis must decide whether an injury is of sufficient degree to require the player to leave the field.

In view of the fact that many injuries in contact sports are recurrences of prior injuries, one must emphasize the importance of proper preventive measures to reduce the incidence of recurrent injuries. It should be noted that the use of procaine (Novocain) hydrochloride or some of its derivatives with hydrocortisone and hyaluronidase has been known to cause complications. I wish to cite a case from the records of Dr. Carl Badgley, professor emeritus of orthopedic surgery, University of Michigan, Ann Arbor.

TABLE 5.—*Body Distribution of Injuries Incurred in Sports at Harvard University**

Region	1932-1937	1937-1942	1942-1947	1947-1954†	Totals
Abdomen	18	10	1	8	37
Achilles tendon	31	5	3	4	43
Ankles	344	200	125	226	895
Arms	38	35	12	15	100
Back	87	57	5	32	181
Buttocks	29	10	0	3	42
Calves	147	91	48	14	300
Chest	75	48	55	35	213
Crotch	27	0	0	1	28
Elbows	53	38	21	12	124
Face	228	122	44	48	442
Feet	187	68	39	45	339
Groins	114	108	39	21	282
Hands	288	109	55	41	493
Head	182	109	71	140	502
Heels	32	8	2	3	45
Hips	58	26	0	4	88
Knees	426	301	137	273	1,137
Iliac crest	30	29	24	28	111
Neck	20	14	1	11	46
Shins	54	16	7	60	137
Shoulders	212	189	64	129	594
Teeth	14	1	0	11	26
Thighs	416	240	113	142	911
Throat	11	6	6	15	38
Viscera	35	42	16	12	105
Wrists	51	32	21	31	135
Totals	3,207	1,914	909	1,364	7,394

* From Thorndike,[1] p. 137.
† For seven academic years rather than five.

This 19-year-old college football player was first seen July 29, 1957, for painful swelling below the medial malleolus of his right foot. He was seen in consultation at the request of the boy's father. The doctors at the college had placed his leg in a plaster cast for one month four months previously; after removal of the cast there was considerable improvement in function of the leg, without pain. However, on resuming physical activity he had a recurrence of symptoms. Physical examination revealed ½ in. atrophy of the right calf and locally there was definite thickening of the tissues about the posterior tibialis tendon behind the malleolus; the functional testing of this muscle caused pain localized in this area. Anteroposterior, lateral, and mortise x-rays "failed to

reveal any abnormality." In view of the fact that this patient had had multiple injections of procaine and hydrocortisone in this area, the diagnosis of chronic tenosynovitis was made and operation for release of the tendon sheath was recommended.

At operation on Aug. 2nd this diagnosis was confirmed, and crystalline deposits were found in the area explored. An interesting laboratory finding was a high blood uric acid level. In view of this finding, he was seen by consultants to appraise the possibility of gout. He played football this past fall with continued symptoms somewhat alleviated temporarily by frequent injections of procaine hydrochloride. After the operation the patient was seen in December, 1957, and January, 1958, and in the evaluation by the arthritis unit of the University of Michigan no specific diagnosis of arthritis could be proved. Laboratory tests failed to reveal any elevation in the blood uric acid level. Diagnosis was tendinitis of the right posterior tibial tendon.

Summary

With the great increase in sports participation in schools and colleges, it behooves those interested in reducing the incidence of injury in sports to organize sufficiently accurate reports of types of injuries and the disability period of each. To determine the true incidence of injury in sports on a national or regional basis, we must record and report. Each sports participant should be conscious of his "bill of rights."

Coaches of high school and college teams should be relieved of responsibility for all athletic injury, and a team physician should be present at all contact sports sessions, whether practice or game. He, and he alone, must assume all medical prerogatives.

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PROTECTING THE BOXER

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It is possible to prevent death and severe disability in boxers by enforcing certain medical standards and requirements. These include an adequate medical department, basic medical examination of boxers, adequate supervision and equipment at the ringside, periodic examination and retirement of boxers handicapped by previous injuries, semiannual physical examination of referees, and annual examination of judges. Boxers in New York state must be licensed on the basis of rigid annual examinations, and two physicians are required to be at the ringside for all bouts in that state. Systematic research into types and causes of injury, especially to the brain, the kidneys, and the skin, has led to substantial gains in safety. These gains are manifest not only in recent statistics for injuries and mortality but also in the liberalization of policies granted to boxers by insurance companies.

Boxing is truly an international sport whose members represent many creeds, races, religions, and nationalities. Its popularity and wide appeal in this country have made it the great American pastime of contemporary sports. It is classified as one of the so-called body-contact sports, along with baseball, football, basketball, hockey, and other similar games, during the performance of which actual body-contact occurs. In boxing, this contact is not only more frequent but often more severe and, on occasion, serious injuries or, rarely, a fatality may result. Thus, boxing has often been considered the most dangerous of all the competitive sports.

Until recently, little thought or concern was given to the safety and welfare of the boxer, in or out of the ring. Many factors contributed to this apathy and apparent negligence, the most important of which was that the very nature and concept of the sport were such that any added measures, other

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than the boxers' physical endurance and ability, were not only unnecessary but harmful to the best interests of boxing. The serious injuries incurred in boxing have too often been accepted and explained as unfortunate but unavoidable accidents, inherent in the sport.

The time-honored skills in which the art of self-defense and offense are basic remain the most reliable weapons in the protection of the boxer in the ring. There is no genuine substitute for these defensive skills and offensive tactics, and they can be attained only by a carefully planned and supervised boxing program. Relatively few boxers, endowed with natural ability and athletic talent supported by adequate training and experience, have been so fortunate as to escape serious injury during their ring careers without the aid of additional safety precautions and medical supervision.

The amateur is generally more closely supervised and carefully protected than the professional boxer. The protection which is so necessary to the amateur boxer in this developmental stage of his ring career is in direct proportion to the intimate relationship with and the personal interest given him by his local club or the social or religious organization through which he is sponsored.

The professional boxer is not so fortunate, and for years professional boxing has universally been considered the most dangerous and risky of all the competitive sports. There will always remain a small but persistent minority who sincerely believe that the dangers and disadvantages inherent in boxing far outweigh any positive values claimed for the sport and that it should be abolished. Many sports authorities and physicians mistakenly believe that the incidence of fatalities and serious injuries is greater in boxing than in any of the other body-contact sports.

Gonzales,[1] in a report of fatalities in competitive sports based on a study over a 32-year period from 1918 to 1950, found that there were more deaths in both baseball and football than in boxing during that period: 43 in baseball, 22 in football, and 21 in boxing. His conclusions based on that study were that "32 years of boxing competitions have produced fewer deaths than occur in baseball or football, in proportion to the number of participants, and far fewer deaths than result from daily accidents. It seems that the moral and physical benefits derived from boxing far outweigh the dangers inherent in it or any of the other competitive sports."

The nature, methods, and objectives that have traditionally been identified with professional boxing have been considered so absolute and all-important that any medical supervision or measures for the protection of the boxer have often been reluctantly accepted by him or rejected by those promoters in charge of boxing. The old concept of winning at any price or "going down like a champ" has all too frequently exposed the boxer to unnecessary risks and serious injuries. An equally untenable and inhuman practice of permitting the fight to continue just for the sake of pleasing a few irate and frenzied fans at ringside, even though it is apparent to any impartial observer that a catastrophe is imminent, has produced mounting criticism and disfavor of the sport.

From 1946 to 1951, seven deaths occurred among professional boxers in New York state. This was a marked increase over former years and it clearly revealed the need for better medical supervision and more adequate safety precautions in professional boxing. Unfortunately, there has been little interest shown by physicians and sports officials, or by the medical profession generally, in the medical aspects of professional sports.[2] This applies particularly to boxing, in which there are no available statistics or data sufficiently accurate or informative enough to be of value in determining the medical status of boxing, past or present. Furthermore, there are factors inherent in boxing which have made it difficult to plan or establish any long-range or satisfactory medical program for this sport. Unlike baseball, football, and basketball, which are seasonal team sports, boxing is an individual, year-round sport and the average boxer is a globe trotter and does not confine his ring activities to any one state or locality.

New York State Athletic Commission

In New York state, professional boxing, since 1920, has been under the supervision and control of the State Athletic Commission, appointed by the governor. The chairmen and other members have consistently been men of outstanding ability and accomplishments in government, business, law, and sports. Their contributions to boxing have been many and varied, and the great strides and advancements which have been made in this sport over the past 35 years have been made possible largely because of the commission's humane interest in and deep concern for the personal safety and welfare of the boxer.

Up until 1948, the local clubs and the boxers' managers assumed the financial responsibility for the medical welfare of their boxers. The commission approved physicians who examined the boxers and acted as ringside doctors and were experienced and capable men, many of whom have spent most of their professional careers in boxing. Dr. Vincent Nardiello was the dean of boxing and ringside physicians until his voluntary retirement in 1957. He has unquestionably examined more boxers and served as ringside physician at more bouts than any doctor in ring history, and he has properly become the family doctor and medical adviser to a number of boxers and sports officials identified with boxing. It is largely due to the untiring efforts and services rendered by such dedicated physicians that many boxers have been spared from serious injury and disability during their ring careers. Moreover, their contributions to the medical phase of boxing has made possible much of the progress which has been made in professional boxing today.

As in other sports and occupations, the performance of which may be hazardous and dangerous at times, a decision had to be made concerning the future of boxing in New York state. Skepticism and doubts by many sports-minded individuals and groups and ardent boxing fans were expressed. Further opposition by those who have traditionally opposed boxing in any form, insisting that it could never be made a safe and humane sport, served only to confuse and prejudice the thinking of fair-minded and impartial officials. Against this confusing background was the usual problem of the cost and financial responsibility of any worthwhile medical program for boxers. The boxer could not afford to and the clubs and promoters could not be depended upon to finance and maintain such a program.

Fortunately for boxing, the state expressed its complete confidence in the sport and faith in the boxer, as it had on previous occasions when the future was threatened. It accepted its responsibility for and discharged its obligations to the boxer by the appropriation of the necessary funds for the establishment and maintenance of the first comprehensive long-range program for boxing. A brief outline and discussion of the organization and functions of the medical department and its accomplishments over the past six years, during which time most of its measures and recommendations were in operation, form the basis of this report. Included is a statistical study of the medical results achieved in boxing during this six-year period, from 1952 to 1957.

The first medical advisory board for boxing was formed in New York when Governor Dewey appointed this body in 1948. It consisted of nine members, including a chairman all of whom are outstanding specialists from medical schools and leading hospitals in the state. These authorities in sports medicine included a neurologist, psychiatrist, orthopedist, ophthalmologist, internist, physician in industrial medicine, surgeon, and dentist. While, theoretically, this board was primarily created to serve in an advisory capacity, the athletic commission wisely recognized and respected the scientific and medical achievements of this board to the extent that it was given the responsibility and authority in establishing and maintaining a comprehensive medical program for boxing.

Under the leadership of the present chairman, Dr. Marvin A. Stevens, an orthopedic surgeon who for years was a prominent football coach and is a recognized authority in sports medicine, nearly all of the many medical recommendations and safety measures sponsored by the medical advisory board have been approved and adopted by the commission. Most of this program has previously been reported in outline form.[3] Hence, only those measures which have been either omitted or only briefly mentioned and have real merit will be stressed.

Medical Standards for Boxing

Medical standards and requirements for boxing are (1) a modern, adequately staffed and equipped medical department, (2) basic standards and requirements for the medical examination of boxers, (3) adequate medical supervision and equipment for the boxer at ringside, (4) periodic examination and evaluation of poor medical and boxing risks, and, (5) semiannual physical examination of referees and annual examination of judges. There are now 36 commission-approved physicians for the examination of boxers in New York state. There are two full-time, trained technicians who take x-rays, electrocardiograms, and electroencephalograms and do the routine laboratory work required on boxers and officials. The medical department is completely equipped with all the facilities and instruments necessary for the physical examination of the boxer.

Each boxer before being licensed to box in New York state must receive and pass a rigid annual physical examination, including routine x-ray of heart and lungs, electroencephalogram, blood and urine examination, and other special examinations as indicated. Special attention is given to examination of the eyes, and there is a minimum requirement of 20/100 vision in either eye (which can be corrected to normal with glasses) with no demonstrable pathology in either eye. Additional routine examinations include the five-day prebout physical, noon-day weigh-in, and immediate prebout and postbout examinations. These findings are recorded on appropriate record and injury report forms. Special attention is given those boxers who sustain a knockout and they are required to have a neurological examination and an electroencephalogram before reinstatement.

Since 1952, two physicians are required to be at ringside for all bouts in New York state. They are supplied with a well-equipped medical kit containing first-aid dressings, suture materials, antiseptics, and appropriate drugs for the resuscitation and emergency treatment of the injured boxer.

All boxers who are susceptible to recurrent injuries or who sustain six or more consecutive losses are carefully evaluated by the commission and reexamined by the medical department. Such individuals are considered candidates for serious injury, and accordingly most of them have been medically disapproved by the board and retired by the commission. It is felt that this precautionary measure has saved many boxers from serious injury or possibly a fatality in the ring. Another valuable safety measure to spare the boxer further and possibly more serious injury is the timely intervention by the referee in stopping the fight on either his decision or that of the ringside physician. Even today far too many fights are allowed to continue when the boxer is helpless, with his arms dangling at his side and taking an unmerciful beating by his

opponent. Such an uneven and one-sided contest should be halted minutes earlier rather than seconds later.

Safety measures and equipment required at ringside include (1) a new type ring padding replacing the old felt pad, (2) substitution of 8-oz. for 6-oz. gloves for all except championship bouts, (3) properly fitted mouthpieces to be worn by the boxer during the fight, (4) a portable resuscitator with oxygen equipment, available at all rings, and (5) 30-day automatic minimum suspension for any boxer who sustains a knockout, technical knockout, or other injuries of sufficient severity.

The replacement of the old felt padding by the new plastic ensolite fiber board pad (the result of over two years of exhaustive research), under the ring canvas, has largely eliminated the fatalities from serious head injuries, which were so prevalent when the old felt pad was in use. There is no longer in evidence the back and forth rocking of the head on impact of the occiput against the ring canvas which was commonly observed before this new type of pad was introduced. It is generally believed that this so-called acceleration-deceleration phenomenon which resulted from a knockout, as previously described, was the cause of those direct and contrecoup injuries and serious hemorrhages in the brains of boxers. Certainly, the incidence and severity of head injuries in boxers have been significantly fewer since this safety device was introduced.

The automatic 30-day minimum rest period, which is also honored by all states and municipalities who have a reciprocal working agreement with the New York Athletic Commission, prevents the injured boxer from getting back into the ring before he has been pronounced physically fit for fighting. The various commissions are simultaneously notified by bulletin when the boxer has been medically approved to resume fighting.

Clinical Investigation of Trauma

Clinical investigation and studies of various types of trauma associated with boxing include (1) ringside study of knockouts and frequency of head blows correlated with neurological examination and electroencephalographic patterns, (2) examinations before and after bouts to determine urologic trauma, and (3) comparison of the abrasive and irritant effects of rosin versus calcium carbonate.

The study of "Observations on the Clinical and Brain Wave Patterns of Professional Boxers," by Kaplan and Browder,[4] was reported in 1954 before the section on nervous and mental diseases of the American Medical Association. This marked the first attempt of any experienced neurologist to observe and study at first hand during the progress of a fight, and immediately thereafter, the average number of blows to the chin and head of boxers in the course of a fight and the pathophysiological changes which contribute to and result from a knockout. Kaplan served in the capacity of ringside physician while conducting these investigations, and in addition to his detailed observations made movies including slow-motion pictures of many encounters, with special emphasis on head blows, in particular those producing knockouts. He noted that most of the blows aimed at the chin or head were either blocked or fell far short of their mark.

His observations and deductions concerning the most probable causes of a knockout and unconsciousness from a blow to the chin or head are as follows: "A blow from a human being with a padded gloved fist probably is not forceful enough to produce any direct damage to the brain. Most dazed and unconscious states are due to an excessive inflow of stimuli from many sources. I actually believe that boxers become unconscious from a head blow because of the very rapid turning of the head when it is struck, thereby activating the vestibular mechanism to excess. Similarly, a blow to the abdomen may produce stimuli to the nerves in that area and cause an excessive inflow of impulses to the reticular area of the brain stem. When the cells in the reticular mechanism receive this tremendous bombardment of incoming nerve impulses, they may block off for a period of time. Any severe pain can cause a person to become unconscious in a similar manner. This may be a protective mechanism on the part of the body. I realize that this is highly theoretical, but it is certainly as good as any of the present day theories." [5] Certainly, Kaplan's observations and deductions are based on an abundance of clinical and laboratory data, as there are now available over 3,000 serial electroencephalograms in boxers. He has challenged the so-called punch drunk syndrome, originally described by Martland [6] in professional boxers, and more recently revived and emphasized by Jokl.[7] Kaplan believes that the clinical picture and pathological findings associated with this syndrome are not peculiar to boxers but have been found in the average populace as frequently as in professional boxers.

There have been two excellent studies of urologic trauma in boxers; one is a report on acute renal trauma in boxers by Amelar and Solomon.[8] They reported on the prebout and postbout urine examinations in 103 professional boxers: albumin appeared in 68%; red blood cells in 73%; and granular or hyaline casts in 26%. They concluded that the effects of acute renal trauma sustained during a fight can be determined in part by an appropriate urinalysis and that further investigations were indicated on a broader basis to determine the true incidence, severity, and effects of urologic trauma in boxers.

The other and more complete investigation of urologic trauma in boxers was conducted by Kleiman,[9] a urologist. He analyzed the results of his studies of 764 boxers over a three-year period and stated that there should be a thorough clinical and laboratory investigation of any candidate for boxing who has a history of any genitourinary disorder or renal pathology. Excretory urography should be included, when indicated. Kleiman con-

clusively demonstrated that trauma to the kidney by boxing, when superimposed upon preexisting pathology or anomaly, may justify the retirement of the boxer because of the likelihood of serious renal damage. In contrast, in a study of 20 retired boxers, a complete urologic survey did not reveal any pathology that would not ordinarily have been present in any similar group of nonboxers.

Dr. Max Moses[10] performed experiments in determining the relative superiority of calcium carbonate (talc) versus rosin as antislip agent and as to their respective irritating properties in the eye and on open wounds. Adult albino rabbits were used. His conclusions were that while calcium carbonate was slightly less irritating to the eye and in wounds, it produced a foreign body reaction and was more difficult to remove. Rosin was far superior as an antislip agent, and over-all rosin is superior to calcium carbonate and should not be replaced by it on the ring canvas.

Medical evaluation and statistical report of a six-year study, 1952-1957, of professional boxing in New York state revealed that of 9,871 participating boxers there were 259 knockouts, 718 technical knockouts (502 as a result of injury and 216 from inability to defend self), 9 serious head injuries requiring hospitalization, 16 eye injuries (11 corneal injuries and 5 detached retina), 29 fractures (12 metacarpal, 11 nasal, 3 of the jaw [mandible], and 3 of the phalanges), and 4 dislocations of the shoulder; 138 boxers retired or were denied license, and there were no deaths.

The absence of mortality or serious injuries in boxers during this period (there were seven deaths in the six-year period just preceding this study) is gratifying and indicates that these favorable results justify the belief and confidence in a medical program as outlined which has proved adequate for the maximum safety and welfare of the boxer. This confidence has been further demonstrated by the sizable increase of medical benefits from $500 to $750 and death benefits from $3,500 to $7,000, and these were effected without any increase of premium rates to the boxer.

Summary

The New York State Athletic Commission and its medical advisors have advocated and adopted medical measures and recommendations for the safety and welfare of the boxer. These many and varied medical measures, safety precautions, standards, and requirements, including clinical studies and research, can make boxing safer. The absence of mortality and the relatively few serious injuries in this group (less than that observed in other body-contact sports), as revealed by the medical statistics involving 9,871 boxers who actively participated in boxing during the six-year period, 1952 to 1957, when this program was enforced, strengthens confidence in the efficacy of this program in the protection of the boxer. Professional boxing can survive and prosper under such a program.

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The Cornell Aeronautical Laboratories of Buffalo, N. Y., produced the plastic ensolite fiber board pad. The Lederle Laboratories, Division of American Cyanamid Co. of Pearl River, N. Y., made the experiments on rosin versus calcium carbonate for the ring canvas.

Miss Alice Oliveri and Miss Kathy Holadak performed the laboratory and technical work for this study.

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PENETRATING RADIATION FOR CANCER.—Since there has been no significant increase in cancer cure rates in recent years that can be attributed to the treatment method alone, new and more radical procedures have been introduced in an effort to improve the results. In radiation therapy this has taken the form of supervoltage generators and the use of high energy sources of radiation such as Cobalt 60 and Cesium 137. As this trend gains momentum, the place and future of orthovoltage therapeutic radiation (250 to 400 kilovolts) must be considered. General agreement is that supervoltage radiation offers an increase in depth dose and fewer local and systemic reactions, but it is too early to assess any change in cure rate. Measured against this is the danger of deep tissue damage, less relative biological efficiency and increased costs. In view of our ignorance regarding cancer, abandoning proved procedures prematurely is unjustified. The most promising trend lies in improved training and in the skillful use of what we have.—S. R. Baker, M.D., Orthovoltage Therapy, *California Medicine*, December, 1958.

PREVENTION AND TREATMENT OF SKI INJURIES

Hans Kraus, M.D., New York

Injuries are less frequent in skiers who are in good physical condition, are skilled, and have good equipment. The treatment of most injuries in skiing mishaps is based on general orthopedic principles, but the idea of immediate mobilization needs to be emphasized. If pain and muscle spasm make mobilization difficult, the necessary exercise can generally be given after use of an ethyl chloride spray on the painful area, provided major ligament tears are excluded. There is no adequate explanation for the deep effect of the surface anesthesia, but the pain-free interval can be used to restore the muscle to normal function. Four case histories illustrate the complete rehabilitation of patients with fractures of the humerus, pelvis, and ankle and partial tear of the medial collateral ligament of the knee.

Skiing is here to stay. Its ever-increasing popularity can be witnessed by the number of ski resorts and lodges that have sprung up in all parts of the United States, by the special trains and other transportation facilities provided when "conditions" are right, by the publications devoted to this subject, by the endless conversations of the ski enthusiasts, and by the fact that, even if Nature doesn't provide snow on the slopes, man will make it!

Yes, skiing is here to stay—but with it comes the problem which is the subject of this paper, namely, the "ski injury." There are two main causes of injury: lack of skill and lack of proper physical condition. The prevention and the treatment of ski injuries create a definite and interesting problem to any physician in the United States today.

The value of the lessons learned in the treatment of ski injuries exceeds the particular application. It can be used to great advantage in the management of other athletic injuries, as well as occupational injuries.

In an effort to supplement available literature and our own experience, questionnaires were sent out to a number of physicians in skiing resorts, to ski patrol men, to ski schools, and to prominent skiers. The answers received [1] added substantially to our information on the cause and prevention of ski injuries.

Athletic injuries are those produced by circumstances inherent in respective athletic performances. They are, therefore, characterized by exposure to recurrent identical trauma and strain, making reinjury likely. Treatment includes managing the injury itself, avoiding recurrence, and permitting return to the activity as soon as possible.

Ski injuries in particular show very typical recurring hazards, which can be dealt with and which can be minimized. Since skiers usually insist on returning to their sport as quickly as possible and since this invariably offers an opportunity for identical trauma, an interesting treatment problem is presented, primarily in the phase of rehabilitation; that is, restoration of function to the greatest possible degree in the shortest possible time.

Just as rehabilitation of the ski injury deals primarily with restoration of muscle function (i. e., normal strength and flexibility in injured part), prevention of ski injury deals with assuring the skier of minimum physical requirements for safe conduct of the sport.

It is difficult to prove to what degree the physical condition of a skier is responsible for accidents. Figures available have to be evaluated with care. However, some definite information points to the fact that good physical condition is extremely important. Two instances may serve as illustrations: 1. A Westchester, N. Y., ski club averaged 5,000 skiing days during 11 years. During this time pre-ski conditioning was practiced. No fractures, and only two mild sprains, occurred. When the pre-ski conditioning was given up, three fractures occurred during the first year. 2. At the North Country School, Lake Placid, N. Y., similar facts are shown. An enrollment of 50 children, aged 8 to 14 years, accumulated a total of 5,000 skiing hours. Seven fractures and five sprains occurred. When a pre-ski conditioning program was adopted, none of the children participating in the program suffered accidents in the first year (5,000 skiing hours); two boys who did not do conditioning work suffered fractures of the leg.

The fact that ski injuries occur rarely in ski schools is well established. At the Mt. Mansfield Ski School only one fracture occurred in 7,310 hours of instruction, and in Switzerland there was only one "accident" in 3,498 hours of instruction.

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Read in the Symposium on Sports and Sports Injuries in the Session on Injury in Sports before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

Prevention

The most important factor in preventing ski injuries is the skier himself. Most ski injuries are due to insufficient know-how or to poor physical condition of the skier. Speed, snow conditions, visibility, and trail conditions are hazards only when they are not properly recognized and managed.

The statistical evaluation of ski injuries is more difficult to ascertain than that of any other athletic injury. In order to compare figures accurately, they would have to be computed in terms of downhill feet, and though this has been done in some instances even this computation compares unequals; 1,000 ft. of downhill run by an expert cannot be compared to the amount of skiing done by a beginner or a racer.

It is obvious, even to the uninitiated, that equipment plays an important role in the prevention of ski injuries. A survey, supported by most personal opinions, reveals that, while release bindings are by no means safety bindings, they do offer a worthwhile improvement on the chance of avoiding injury. At Garmisch-Partenkirchen, Germany, of 17,500 persons who rented nonrelease bindings, 74 sustained fractures; of 45,043 who rented release bindings, 11 sustained fractures. At Stowe, Vt., nonrelease bindings were used by 48% of skiers, in which group 66% of accidents occurred.[2] Also, the use of less pointed poles would decrease some of the stab injuries. Sharp edges have increased the incidence of cuts, but it is unlikely that this, even if generally known, would persuade any skier to make a change.[1c] Clothing and boots have now been generally developed to the point where most skiers are properly protected. And, since skiing areas are usually close enough to warming facilities, frostbite is not a serious hazard.

As mentioned, strength and flexibility of the skier play the largest part in avoiding injuries by making fatigue less likely and by improving the ability of the skier to meet inevitable spills.[1] A physically adequate skier will know when he is warmed up and will consciously try for warm-up by some uphill walking and cross-country running, and this same skier will realize when he is tired and will avoid that famous last run.

Treatment

Formerly the injured skier came in with the question, "Can I ski again?" Now, even the more severely injured come in with the question, "When can I ski again?"

The management of ski injuries, which, of course, basically rests on generally accepted orthopedic principles, is thereby given an added problem, namely, how to restore full function in the shortest possible time. Attempts to answer this demand have resulted in experience valuable in the treatment of other athletic injuries as well as occupational injuries. The special problem of ski injuries is one of rehabilitation and, more specifically, one of restoration of muscle strength and flexibility.

Clay Ray Murray and William Darrach used to say that the ideal treatment of fractures would be to "wish the bone back in place, to keep them there by a wish, and to start active motion of the injured parts at once." It is this principle that made them advocate open reduction and internal fixation wherever possible. The best treatment is immediate mobilization, not only where internal or external fixation have been necessary but also where immobilization can be eliminated by immediate active measures.

A contraindication to immediate movement is pain and subsequent muscle spasm. Use of local measures in treating the pain and spasm make it feasible to immediately mobilize not only sprains and strains but fractures as well if the position is acceptable and displacement does not have to be feared.

Fractures treated by immediate mobilization include fractures of the pelvis (os pubis), fractures without displacement of the short bones of the foot (intraboot injury),[1a] fractures of the head of the humerus, fractures of the metacarpals, fractures of vertebrae, if uncomplicated and if no pedicles are involved,[3] fracture of transverse processes of vertebrae, and fractures of the ankle without displacement of the lateral malleolus, if not combined with ligament tear. We prefer immediate mobilization for reduced dislocations of the shoulder and elbow, and for fractures of the tuberosity of the humerus. At New York University–Bellevue Medical Center fractures treated over a period of about two years included impacted humerus (87), pelvis (62), vertebrae (47), metatarsal (63), calcaneus (43), and tibial plateau (38).

Immediate mobilization of sprains of the ankle and knee and strains of the lower part of the back, of the calf, or of the hamstring tendons restores function [4] in a shorter period of time, and if followed by adequate therapeutic exercises produces better long-range results. Of 126 persons with injury of the medial collateral ligament of the knee, 51 (40%) had had previous injury. Of 70 who were followed for from 2 to 15 years, none had reinjuries, 62 had skied again, with no complaint, 5 had not skied again, and 3 had skied again, with reactions of pain and swelling.

Before deciding on immediate mobilization, however, it is important to exclude major ligament tears, especially in ankle injuries (fig. 1). Tears in the collateral ligament or intraosseal ligament as well as tears of the medial collateral ligament or cruciate ligament of the knee are not to be classified as sprains. They frequently need surgical re-

pair, sometimes immobilization in plaster casts. The following case histories may serve as illustrations.

Report of Cases

Case 1.—The patient fell while skiing on March 3, 1956. X-rays showed comminuted fracture of the anatomical and surgical neck and greater tuberosity of the right humerus.

Fig. 1.—Serious injuries, drawn from x-ray negative. *Left*, lateral collateral ligament; *middle*, inferior tibiofibular ligament; *right*, medial collateral ligament. (Supplied by Charles Neer.)

He was seen in consultation by Dr. Frank Stinchfield. At his suggestion immediate mobilization was started. The patient came to see me on March 9 for the first treatment, which consisted of surface anesthesia and exercises. On March 23 there was no pain and abduction was possible to 90 degrees and scapula-humerus abduction to 80 degrees. There was steady improvement. On May 18, 1956, there was some limitation of inward rotation but otherwise full range with slight residual weakness. The patient had been skiing since three weeks after the accident without discomfort. On reexamination Nov. 30, 1956, he had full range and power, with no complaints. At follow-up examination there were no complaints (fig. 2).

Case 2.—The patient fell while skiing on Dec. 29, 1948. This patient was placed in a hammock at a local hospital. X-rays showed evidence of fracture of the pelvis with fracture site located in the inferior ramus of the pubis and at the junction of the superior ramus of the pubis with the ischium, both on the left side. Traction was suggested. The patient could not void and was extremely uncomfortable. I saw the patient on Dec. 30, 1948. Therapy was started immediately with ethyl chloride spray and exercises. Immediately after removal from the hammock and start of active motion exercises and ethyl chloride spray, the patient improved and voided spontaneously. On Jan. 3, 1949, partial weight-bearing was permitted and gradually increased. Two weeks after the accident the patient returned to college. On reexamination Jan. 31, 1949, there was no atrophy and the patient had no complaints. At follow-up examination there were no complaints. The patient is able to ski.

Case 3.—The patient fell while skiing on Feb. 26, 1953, and suffered a fractured ankle. Stress pictures showed some medial displacement. The patient was a ski instructor, therefore surgery was recommended (Dr. Frank Stinchfield). There was a complete tear of the deltoid ligament which was repaired, and a Rush nail was inserted to the lateral malleolus. The patient's ankle was in a plaster cast until March 10th, then was placed in half-shell cast. The exercise regimen was supported by electrotherapy. On March 31, 1953, the patient had full range of motion with exception of some limitation of *Vorlage* and inversion. Treatment was continued until April 1st when the patient left New York with his leg in a short leg brace. There was almost full range of motion in the ankle joint and good strength. At follow-up examination in February, 1958, the patient stated he had been skiing ever since with no difficulties (fig. 3).

Case 4.—The patient was first seen on Jan. 25, 1939. He had fallen while skiing and twisted his right knee eight days prior to visit. The history revealed a football injury 10 years previously with repeated episodes of knee injury with swelling. The present diagnosis was partial tear of medial collateral ligament, considerable effusion, and marked vastus atrophy. The patient came in daily for ethyl chloride spray and exercises and was free of pain by Feb. 2, 1939. He skied again, against advice, on March 2nd and returned from skiing with some pain and swelling. Treatment was resumed. Operation was considered but the patient wished to continue on conservative regimen. He improved on therapy with exercise and ethyl chloride spray and was almost fully rehabilitated by May 27th. This patient has been followed closely, as he has returned with various other ski injuries. However, he has had no further difficulty with the treated knee.

Comment.—This patient had had a number of injuries to the knee joint. These episodes ceased entirely after rehabilitation to complete strength.

Technique of Immediate Mobilization

The technique of immediate mobilization includes local relief of pain and therapeutic exercises as the most important factor in the treatment of athletic injuries.[3] A brief description of the technique follows.

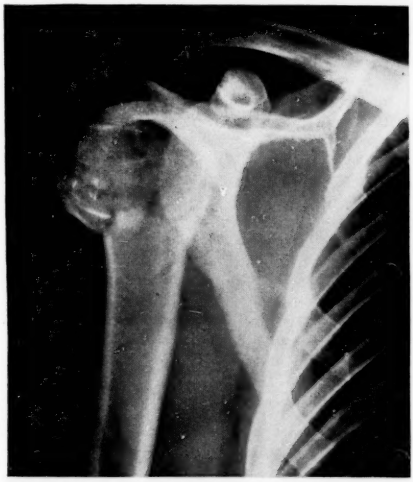

Fig. 2 (case 1).—Comminuted fracture of anatomical and surgical neck and greater tuberosity of right humerus.

The pain is located by active motion. Ethyl chloride is then sprayed on this area. The patient then starts active movement of the part involved, in the direction in which motion has been painful and limited. As the patient increases his range, new painful areas will develop. These areas must again

be sprayed, and active motion continued. Treatments last from 10 to 30 minutes, and should be carried out within limits of pain.

Immediate use of the affected part may be allowed in patients able to perform normal movement, but excessive strain and sudden movement should be prohibited. Patients with more severe disabilities should be advised to rest, but all patients should be urged to continue the active movements that they have been taught. The exercises should be performed from a minimum of twice a day to as often as once every hour, for approximately five minutes. While a single treatment will suffice in cases of minor involvement, patients with more serious difficulty require frequent treatment: daily during the first week and later every other day (fig. 4).

An effective treatment should not require the application of anesthetic after the second week. Therapeutic exercises must continue, and increase in scope, until normal muscle power is restored. Once motion is instituted, immobilization should not be used, as it is contrary to the basic principle. It should be stressed that active motion, though unquestionably necessary, should never be brusque or abrupt so that painful spasm in muscles will not be further aggravated.

Compared with injection of procaine hydrochloride into the muscles and ligaments, the use of ethyl chloride has certain definite advantages: 1. The application is simple. 2. Repeated application is possible with minimum difficulty and risk. 3. Large areas can be controlled that would otherwise require quantities of procaine hydrochloride. 4. Ethyl

Fig. 3 (case 3).—Fracture of distal end of fibula, with fixation.

chloride does not mask bone or ligament injury. 5. It is better as a diagnostic means, since it is more selective. 6. There is less risk of a local after-effect and there is no general after-effect, such as occasionally occurs after the administration of procaine hydrochloride. 7. There is no danger of infection.

The administration of surface anesthesia is only the first step in the treatment of painful muscle spasm. Exercise is the necessary second step. Without it, the use of surface anesthesia would accomplish little more than the use of gas or ether in surgery without operation.

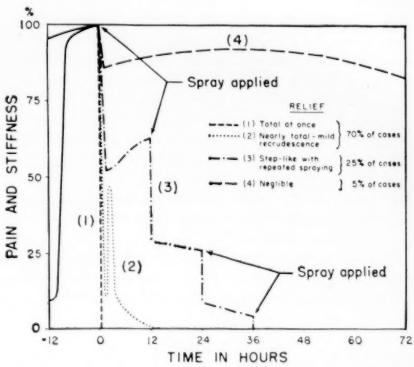

Fig. 4.—Response of acute "stiff neck" to ethyl chloride spray. (Reproduced from Travell,[34] with permission of *Archives of Physical Medicine and Rehabilitation.*)

Exercises must be performed immediately after application of the anesthesia. These should be exercises to restore elasticity and increase relaxation and length of muscle and should always be performed below pain and fatigue limits. Scattered dosage from two to five minutes, and exercises every one-half to one hour should follow. The supporting prescription may call for particular or complete rest between exercises.

The most common mistakes made in treatment with surface anesthetics and exercises are (*a*) failure to cover the full painful area with anesthetic, (*b*) overdosage of violent exercise, (*c*) neglect of pain limit, (*d*) neglect of home exercises, (*e*) neglect of supportive prescriptions, (*f*) neglect of follow-up treatments, (*g*) failure to explain properly to the patient and to arouse the necessary cooperation, and (*h*) faulty indication.

As to the theory involved: Pain originating in one portion of the sensory motor chain leads to reflex muscular spasm and locking of joints (fig. 5). This sensory motor chain consists of the following elements: Sensory nerve, nerve center, motor nerve, muscle and sensory nerve. Pain originating in the course of this chain leads to muscular spasm. Elimination of pain at any point in the chain results in the breaking of the chain, and, therefore, in relaxation of the muscular spasm. This may be achieved directly by the injection of an anesthetic into the muscle, joint ligament, sensory nerve, or spinal cord.

If the pain-free interval is used to restore the muscle to normal function, spasm does not recur, or it recurs with much less intensity. It has been our experience that, on the basis of this chain, cutaneous anesthesia similarly relieves deep-seated pain in muscular spasm.

There is no adequate scientific explanation for the deep effect of surface anesthesia. However, the underlying physiological reason presents an interesting field for exploration. And, it should again be emphasized that surface anesthesia alone, without active motion, will not achieve good results.

When the acute phase has subsided, strengthening exercises to weak muscles, as well as limbering and stretching exercises to tight muscles, must gradually be increased. To be of value these exercises must exceed easy performance and at the same time should cease before the point of fatigue so as to avoid setbacks.[4a]

As soon as the joint can be moved through full range, weight lifting exercises may be added to resistive exercises; but weight exercises are not a substitute for resistive exercises. The weight tolerated through full range is by necessity smaller than the maximum range tolerated in a particular section of the movement.[4a] Active resistance adjusting to these different potentials can, therefore, give a more efficient and complete workout. As long as there is little exercise tolerance, daily sessions are necessary and should be supplemented by frequent periods of movement at home.

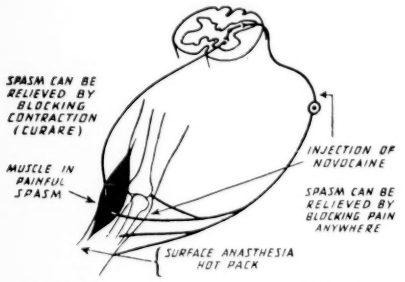
SPASM CAN BE RELIEVED BY BLOCKING CONTRACTION (CURARE)
MUSCLE IN PAINFUL SPASM
INJECTION OF NOVOCAINE
SPASM CAN BE RELIEVED BY BLOCKING PAIN ANYWHERE
SURFACE ANASTHESIA HOT PACK

Fig. 5.—Diagram showing sensory motor chain leading to reflex muscle spasm and locking of joints and method for relief.

Once strong workouts are started, three sessions per week are usually all that are necessary but should be supplemented by homework of one or two tolerance sessions each day. Of course, it is true that such extensive rehabilitation programs should be given only where return to the sport is desired, as one must remember that a knee that is perfect for city life may be in great jeopardy when exposed to the hazards of skiing.

Since it is the lower extremity that is most frequently jeopardized in skiing (see table), evaluation of the injury should include comparison of strength with contralateral side (by weight lift or scale test)[4a] (fig. 6). Full range of knee and ankle joint should be restored. The ankle joint should be especially tested on forward bend with the heel on the ground (*Vorlage*). If this movement is limited, it may well be a cause for reinjury. For example, when a skier goes over a bump and tries to bring his weight forward, he will experience a pull on the shortened muscle. This will cause him to unweight his ski, the tip will tend to dive, and the skier will fall with probable injury to the extremity.

*Distribution of Ski Injuries**

Location	%	Type	%
Head	4.3	Shock	1.1
Shoulder	1.9	Stabs	1.3
Arm-hand	2.7	Dislocation	1.5
Back-trunk	0.8	Fracture	31.5
Leg	92.0	Laceration	10.0
Miscellaneous	0.2	Sprain	51.3
		Bumps, etc.	1.9

*Data from the National Ski Patrol System.

The mere passage of time alone does not contribute to full rehabilitation. It can almost categorically be said that daily activities in the city do not prepare the skier for strenuous use of quadriceps and leg muscles nor do they give the required elasticity of the soleus which makes a leg safe for skiing. A study of 500 skiing injuries revealed that 14.2% were reinjuries. Of 126 knee injuries, 40% were reinjuries. A survey of 195 skiers, by the ski patrol at Stowe, Vt., revealed 132 had had no injuries, 41 one injury, 15 two injuries, and 7 more than two injuries.

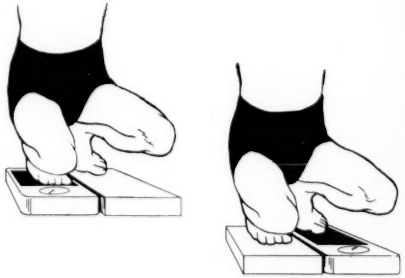

Fig. 6.—Scale test for evaluation of injury by comparison of strength with contralateral side.

Summary

Poor muscular condition is a main cause for ski injury. Physical conditioning before skiing is the best prevention. Weakness and stiffness after injury are among the main causes of reinjury. Therapeutic

exercises to restore full function of the injured part are essential to make it possible for the injured skier to return to his sport safely.

The use of ethyl chloride spray and active exercises immediately after sprains, strains, and certain types of fractures has been found most effective in over 25 years of work with that method.

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RESPIRATORY PHYSIOLOGY AND SKIN DIVING

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Skin diving with self-contained underwater breathing apparatus (scuba) has hazards that distinguish it both from free diving during short periods of voluntary apnea and from traditional diving with helmet, pump, and connecting tubes. It is also necessary to distinguish between the type of scuba in which the expired carbon dioxide is absorbed chemically, the needed oxygen is added, and the nitrogen is rebreathed from the type in which the expired air is simply discharged into the water as bubbles. Although the latter form is less dangerous, it has its hazards, including air embolism, decompression illness, nitrogen narcosis, oxygen intoxication, rupture of eardrums, and squeeze. Squeeze, the pressing of body tissues into air-filled spaces in the diving costume, is particularly damaging to the eyes. The bulging of the eyes into goggles is hard to avoid, but if a mask is worn instead of goggles the danger can be decreased by discharging air from the nose into the mask whenever pressures increase.

Skin diving as a hobby and as a sport has increased tremendously in the past 10 to 15 years. The introduction of commercially available skin diving equipment has increased the number of divers to almost a million people registered in nearly 400 clubs. Skin diving is not limited to salt water seacoast areas. There are many diving clubs even in such inland spots and inaccessible areas (as far as water goes) as the deserts of Nevada and Arizona.

An increase in accidents and fatalities is the result of the marked increase of the number of people who have taken up skin diving. In California there was approximately one death per month from January, 1953, to April, 1955, besides the many accidents which were not fatal. In skin diving the mortality in any given set of accidents is high—in contrast, for example, to skiing, where morbidity is higher compared to mortality. In order to improve the statistics of injury from skin diving, it is appropriate to describe the injuries and accidents which are associated with it and their prevention and treatment.

Read in the Symposium on Sports and Sports Injuries in the Session on Injury in Sports before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

Free diving is diving after a mild or moderate amount of hyperventilation with a deep breath of air and then coming up when the breath-holding period has passed. There is no external source of compressed air or oxygen in this type of diving. In scuba diving (the letters stand for self-contained underwater breathing apparatus), a demand regulator and source of compressed air or oxygen is used and the individual breathes through a flexible rubber hose. In the case of the "compressed air" type of breathing "lungs," the compressed air is inhaled and the exhaust is released through a one-way valve into the water which bubbles to the surface. In the so-called rebreathers, there is a soda-lime chamber to absorb the carbon dioxide, only oxygen is supplied to the bag, and there is no tell-tale bubble trail on the surface.

Requirements for a safe diver include both physical and psychological components. Skin diving can be exhausting, and it is axiomatic that good physical condition is a prime requirement. Good swimming ability is of paramount importance, and familiarity with water sports in general is of tremendous value. No one with chronic cardiovascular or respiratory type of derangement should indulge in the sport. Obesity is also a detriment. Some patients should be limited to free diving in shallow water. The individual who has chronic ear trouble and who is unable to inflate the middle ear through the eustachian tubes with intranasal pressure will find that he can not dive more than 12 to 15 ft. without pain in his ears and the possibility of rupturing the drum.

There are also psychological requirements for a good or, indeed, even a safe diver. The individual who is very nervous, is easily upset, lacks self-confidence, and might panic at the onset of an emergency should never attempt to dive. The show-off type, the dare-devil who takes chances and loves to show his superiority over others, is a dangerous diver whose diving should be controlled as much as possible.

Man's general problems in skin diving are associated with the fact that he is not designed or equipped to be under water safely. The physical laws of gas behavior all impose limits on his underwater activities. Boyle's law is one of the most important. Briefly stated, Boyle's law says that if the temperature remains constant, the volume of the gas varies inversely with the pressure. The pressure at sea level is 14.7 lb. per square inch (760 mm. Hg). For each 33 ft. a diver goes below the surface, there is an increase of one full atmosphere of pressure. Therefore, at 33 ft. there are 2 atmospheres of pressure absolute; at 66 ft., 3 atmospheres; at 99 ft., 4; and so forth.

In this same context, a given volume of air in the lungs (for instance, 2,000 cc. of air) at sea level before diving will be compressed at 33 ft. below the surface to 1,000 cc. and will be compressed another 33⅓% at 66 ft., then occupying a volume of approximately 667 cc. When ascending, a diver at 33 ft. may inhale a breath of compressed air from a scuba unit, filling the lungs exactly half way, and at the surface the lungs will be completely full and the volume of gas will be twice what it was at 33 ft. Dalton's law states that each gas exerts its own tension in a mixture as though it occupied the space alone, and Henry's law states that gases dissolve according to their partial pressures in a contacting liquid. Thus, in general, the difficulty with man under water lies in the air spaces in his body. The body tissues in general are considered to be incompressible, and, in animal experiments, pressures of over 100 atmospheres have not caused noticeable damage to tissues per se.

Air Embolus

The term "air embolus" has been used to describe the accident which occurs when an individual inhales at increased pressures a full lung of air and then rises rapidly through the water to a much decreased pressure, causing a marked increase in the volume, according to Boyle's law, of the compressed air in his lungs. The lung tissue is fragile and, normally, the increased pressure behind the sternum and against the diaphragm can be felt and will usually be compensated for by a normal exhalation, but a person who is in a hurry to get to the surface is frequently in a state of panic. He may also be under the impression that he does not have enough air. A spastic glottis is the result, and the lung tissue can in a mild case be torn and in a severe case be completely ruptured with the introduction of air emboli into the pulmonary veins returning to the left side of the heart. In one case described in the literature, the air emboli were so universally distributed throughout the body that the cut surfaces of all body organs contained air and were felt to exhibit crepitations.

The signs of air embolus are, essentially, bleeding from the lung, shortness of breath, dyspnea, cyanosis, and collapse. In mild cases treatment consists of placing the patient in the head-down position and supportive therapy for shock. At times recompression to the level at which the patient was before he began to ascend in the water is of benefit. Prophylaxis, of course, in such an accident is much simpler and more effective than is treatment. If all divers understood that there is never a situation in which it would be safe to come up to a shallower depth in the water, after breathing compressed air, without a continuously open glottis and free exchange of air in and out of the lungs, such accidents would be much less common.

An interesting side-light in this particular phenomenon has to do with the individual who has, for some reason, been caught at considerable depth with either a malfunctioning scuba or, more usually, a sadly depleted air supply. If he takes a comfortably deep breath at that stage, takes his scuba mouthpiece out, and then exhales slowly at the

greater depths and more and more rapidly as he gets near the surface, he will find that the air in his lungs will be discharged and he will not particularly feel the need of exhaling. This procedure is not essential, necessary, nor indicated in free diving because the diver takes in 1 atmosphere of pressurized air at the surface and dives down to 30 or 40 ft. Then on his way back up the air that was compressed at 40 ft. will expand again but can go no further in expansion than it was at the 1 atmosphere of pressure that he began with at the surface. He took in no compressed air at increased pressure below the surface of the water.

Air embolus can cause death. A diver using a scuba in 20 ft. of fresh water apparently found it suddenly difficult to breathe as the air diminished in his lung. He closed his glottis, kicked for the surface, came up and shouted to the people on shore, but sank again immediately. Postmortem examination disclosed severely shattered lungs. These divers may even die before reaching the surface.

Caisson Disease

Caisson disease (the bends) is caused by increased pressure of nitrogen when one works under pressure. The nitrogen dissolves in the blood stream at a proportion to its partial pressure, according to Henry's law. Then, on decompression from depths, the nitrogen in the tissues and in the blood stream, if not decompressed slowly enough, will cause bubbles which reabsorb slowly and cause what is called "the bends" or "the chokes." Bubbles in the blood stream and tissues cause caisson disease. At 99 ft., at an absolute pressure of 4 atmospheres, nearly 5 cc. of nitrogen is dissolved in 100 cc. of blood; thus, all of the blood of a 155-lb. (70-kg.) man would release 130 cc. of nitrogen and the tissues would release up to 10 times that much. Symptomatology of caisson disease includes pain in over 90% of all cases, associated with the area in which the bubbles are causing difficulty.

The tendons and the cerebral spinal nervous system are two of the most common places that are attacked in caisson disease. The chokes are a manifestation of nitrogen bubble emboli in the pulmonary capillary system with resultant pulmonary edema, usually quite severe. Fat people have more difficulty with caisson disease than do thin people, because of the increased nitrogen solubility in fat as compared to water. The treatment recommended in mild cases is use of recompression to 30 lb. pressure and 100% oxygen at that level for one hour. Then decompression should begin at the rate of 1 lb. of pressure per minute. In severe decompression illnesses, the treatment should be recompression to 75 lb. of pressure, with 50% oxygen, for 15 minutes to two hours, depending on symptoms, and then decompression to 30 lb. of pressure at the rate of 1 lb. per minute and maintenance on pure oxygen for one to two hours. If, however, after 1 hour with pure oxygen at the 30-lb. pressure level, the patient still has symptoms, 30-ft. breathing air is used for 24 hours, then oxygen for 2 hours, followed by 1 lb. per minute decompression rate to normal. Effective treatment in preventing caisson disease is use of a warm compression chamber if no more than three or four minutes have elapsed since the patient left the water and entered the chamber. In one experiment, in 130 dives from 66 to 108 ft. for one-half to two and one-half hours, decompression was begun in an average of six and three-tenths minutes after the divers left the water, and during these dives there were no signs of caisson disease.

For prophylaxis of caisson disease, normal U. S. Navy standard decompression tables are available to the skin diver. Briefly, the depths to which one can dive are estimated from length of time and depth in the water. For example, without any decompression it is generally safe to stay at a depth of 125 ft. for 15 minutes, 75 ft. for 35 minutes, and 30 ft. for any length of time. Time is computed from the moment of leaving the surface until leaving to come up from the greatest depth reached. It is exceptionally difficult to estimate time under water, and only a watch should be considered effective in time measurements. If a diver went 200 ft. down and stayed for 35 minutes, decompression time on coming up would be 22 minutes at 30 ft., 28 minutes at 20 ft., and 46 minutes at 10 ft., with the rise from the bottom at a rate not to exceed 25 ft. per minute, with one minute to come up from the three stops at 30, 20, and 10 ft. This gives 106 minutes of total decompression time from leaving the bottom until reaching the surface. At a depth of 300 ft. for 45 minutes, decompression time would be a total of 5¼ hours at levels from 90 to 10 ft., stopping every 10 ft. One other thing which must be kept in mind in decompression tables is that the effects of any dive which is within 12 hours of the last dive are cumulative, and the diving tables are used by computing the total time of all dives at the last depth. On trips to Catalina, for instance, frequently two or three tanks of air will be used by each diver and caisson disease is likely in a depth of usually 75 to 150 ft. because of the failure of the divers to add their diving times together.

Other Risks of Skin Diving

Nitrogen Narcosis.—The syndrome called nitrogen narcosis or "raptures of the deep" is also a result of pressure of the inhaled air. Below a level of 100 to 160 or 170 ft., depending on the individual, there is a gradually increasing feeling of exhilaration and euphoria, similar to an acute alcoholic bout and described as a feeling of wanting to remove the mouthpiece of the scuba unit and hand it to a passing fish because it is not needed. Fatal errors in judgment may occur as a result of this narcosis. There have been frequent deaths, due partly to this syndrome, of persons who have

tried to break the underwater, deep-diving scuba records. The record at present is in the vicinity of 375 or 380 ft. The treatment for this syndrome is immediate return to shallower depths where symptoms immediately disappear. Prophylaxis is to stay out of the lower depths unless essential. Use of up to 90 or 95% helium with oxygen, used only at the lower depths, will relieve a marked share of the symptoms of nitrogen narcosis.

Oxygen Poisoning.—Oxygen poisoning is the name applied to a syndrome which is the result of breathing oxygen at markedly increased pressures. The depth reached before this syndrome begins varies in different persons, but generally the limit of oxygen for any length of time is considered to be about 30 ft. Some have gone down 40 or 45 ft. for one-half hour without difficulty, but the more exercise that is involved at that level the more is oxygen poisoning likely to occur. Symptoms include dizziness, headache, muscle twitching, and convulsions with coma. This syndrome occurs mainly in the rebreathing units at the shallower levels but may occur in extremely deep dives with the use of air. For instance, at a depth of 297 ft. and an absolute pressure of 10 atmospheres, the use of compressed air or even a 20% oxygen mixture with helium will give the same oxygen partial pressure as using 100% oxygen at 33 ft. Therefore, symptoms below that level can be identical with oxygen poisoning. Oxygen tensions of air which is breathed in the cylinders used in the deep diving record attempts are almost always cut down to 10 to 8% or even, for low dives, 5%, in order to minimize the possibility of oxygen poisoning. The treatment is simply to come up from the depth at which symptoms begin, and they will decrease rapidly.

Drowning.—Drowning as a result of exhaustion, oxygen lack, and carbon dioxide excess is one of the most common sources of fatalities. Exhaustion is the keynote to this type of accident, and the development of the exhaustion would be markedly increased by panic in an emergency which could cause a diver to overextend himself and ignore completely the general principles of safe diving. The symptoms are unconsciousness, cyanosis, and vasomotor collapse. The treatment is immediate and enthusiastic artificial respiration, preferably with oxygen. The prophylaxis of drowning is to remember to have available under all circumstances and at all times as many of the safety precautions and equipment as possible. One of the most effective safety measures is some type of a float with a line on it at least three times as long as the planned diving depth, with a 2-lb. or 3-lb. anchor weight on the end. This float may be an innertube or a fancy arrangement on which one can hang spear guns, fish, abalone, abalone irons, and camera and thus have an efficient piece of equipment as well as a reliable, handy place to rest. There is no way of overemphasizing the importance of having somewhere to rest when one becomes overtired or has had a harrowing experience. Many men have had nearly fatal accidents, and it behooves all divers to use their heads and take advantage of such a simple and efficient piece of apparatus as a float.

Ruptured Eardrums.—The increased pressure at depth is a mechanism which forces the eardrum to go inward toward the middle ear unless there is equalizing pressure from the middle ear to prevent it. If the eustachian tubes are closed off and air is unable to reach the middle ear from the nose, a ruptured eardrum may occur. The symptoms are acute pain in the ear and, frequently, bleeding from the external canal. Treatment is prevention of infection and prohibition of diving until healing is complete, approximately a period of eight weeks. Without infection, complications, or a severe tear, a small rupture will heal promptly and normally without difficulty. Prophylaxis depends on having the eustachian tubes as open as possible and not diving unless they are open and kept that way. Ear plugs should not be used in diving as they would, if they fit tightly, cause a rupture of the drums from the inside as soon as the pressure in the middle ear reached the pressure of the water. The free exchange of pressure into and out of the external ear is just as essential as the exchange into the middle ear through the eustachian tubes. There is an associated condition in which a rubber suit, used for warmth, can flatten out over the external canal, sealing it completely.

If the negative pressure in the external canal with the pressure bowing the drum out from the middle ear is not quite strong enough to break the drum, a blood blister may occur from the suction effect. This blister can be quite large and rupture the skin of the external canal beside the drum, with bleeding from the ear. The prophylaxis is not diving with a severe cold or when for any reason the eustachian tubes are unable to allow the transfer of air back and forth freely. An easy way to test this is to hold the nose tightly and try to blow hard through the nose so that the intranasal pressure is increased. If there are stuffy feelings in both sides through both ears, then the eustachian tubes are open and will present no difficulty. Frequently the use of propylhexedrine (Benzedrex) or some other type of an inhalant to shrink the mucous membranes will give a good exchange where swollen membranes would cause difficulty.

"Squeeze."—The phenomenon known as "squeeze" is peculiar to the use of the dry suit, which is a solid rubber sheeting arrangement encasing the body, with elastic wrist bands and a stretchable opening for the face. Means of entry is a chute in the front of the chest, and this is closed off with rubber bands. Two or three sets of wool underwear are worn inside this rubber suit for warmth. Air entrapped in this underwear by the pressure of the water may cause folding of the

skin, and the skin may actually be sucked up into little ridges and welts in the folds of the cloth because of the relative negative pressure of some of the folded areas. The ridges and welts may approximate blood blisters and last for several days. The areas with the most air entrapped are those of the poorest fit of the rubber suit, especially the genital areas, and in a male diver squeeze may be quite noticeable. Also, air from the scuba unit may be forced into the suit by snorting into the face mask, causing an increase of the amount of air inside. This is all right at 100 ft., but during ascent this same air under pressure blows up the suit like a balloon; the rate of ascent can thus get out of control, so that it may be difficult for the diver to slow to the recommended rate of 25 ft. per minute. This does not happen with a wet suit, which allows water to get inside, thereby equalizing the pressure.

The same type of a squeeze may occur as a result of a tightly fitting face mask if the individual does not realize that he needs air from inside his nose to fill in the mask. Water pressure can compress the mask sharply around the nose, face, and eyes, causing negative pressure with protrusion of the eyeballs. For this reason, in any but the mildest and most shallow of diving, diving goggles are not recommended. They allow no method of putting air inside the goggles themselves when under pressure, and, therefore, eyeball squeeze is more frequent with goggles than with masks.

Comment

These, then, are some of the difficulties which can beset a diver. Diving is a tremendous sport, exciting, interesting, and different. But the sea is a hard taskmistress and she allows comparatively little human error. With adequate preparation and precautions, diving can be safe. Without them, accidents are likely and dangerous. It behooves everyone to be as careful as possible in taking up the wonderful sport of skin diving.

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SURGICAL TREATMENT OF INJURIES TO LIGAMENTS OF THE KNEE

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The most severe forms of injuries to the knee often do not properly heal without surgical intervention. This is true whenever any major ligament is completely cut across or avulsed from its attachment, and particularly when the torn ends of one structure come to lie in positions that hinder the union of other structures. Surgical experience with over 150 cases of injury to the knee has shown that conservative treatment can be expected to lead to healing only when tears are partial. When the symptoms of pain, instability, abnormal mobility, hemarthrosis, and circumarticular effusions testify to severe injury, conservative treatment fails. The best results in such cases have been obtained when diagnosis was precise and surgical treatment prompt. Surgery is followed, on the same day, by physical therapy, which includes muscle-setting exercises (isometric contraction without joint motion) and other graded activities. A policy of complete repair and conscientious rehabilitation has given increasingly gratifying results.

While we are not primarily concerned in this discussion with the over-all treatment of injuries to the ligaments of the knee, one cannot intelligently discuss surgical treatment of such injuries unless there is some generalized discussion of the proper indications for surgery as opposed to nonsurgical measures. I have repeatedly emphasized in previous reports the necessity for an extremely accurate diagnosis of an injury to the knee if one is to be prepared to carry out the ideal treatment.[1] If one assumes that surgical treatment is never indicated for injured knee ligaments, treatment of the injured knee becomes vastly simplified. If on the other hand one is prepared to admit that there are some cases which will require surgical treatment, it becomes immediately apparent that one must be able to determine which case should be treated by surgery and which case should be treated by nonsurgical methods. If all ligament injuries are to be treated by modifications of the same basic method, it may indeed be of only academic interest to try to determine the exact pathology which is present in any given case.

Read in the Symposium on Sports and Sports Injuries in the Session on Injury in Sports before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

I think there is a general agreement that there are certain basic therapeutic measures which should be instituted in the treatment of an injured knee ligament. Individual physicians may use many variations but, in general, aspiration, local injection, compression bandage, ice pack, immobilization, local heat, protection, and finally rehabilitation are utilized to a greater or lesser degree, depending on the severity of the injury and on the inclination of the physician. If all knee injuries are to be treated alike, it may be of little importance to determine the exact pathology, since one can play it more or less by ear and regulate the number and degree of the above measures he uses according to the response of the injury to treatment. This may be the easiest and most convenient way of treating it. The fly in the ointment, of course, is that this is not the best way of treatment.

If one could safely assume that treatment may be standardized into the measures mentioned above, the problem would become quite simple. If there is effusion, aspiration may be carried out. If the effusion recurs, aspiration may be repeated. If the effusion subsides, further aspiration will not be necessary. If the injury is mild, compression may well be the only protective appliance applied, and it may soon be discarded. On the other hand, if swelling persists, compression bandages may be continued over a longer period of time and vary from the elastic bandage to the application of a cotton cast. If symptoms do not subside promptly, more adequate treatment may be carried out to the extent of applying a plaster cast, which can be worn for several months if the knee does not respond. So, if treatment is to be identical whatever the degree of the injury and whatever the ligaments involved, one could well initiate this treatment first and then decide, depending on the patient's progress, whether he was badly hurt or had a minor injury. Why then should we demand "tender but meticulously complete examination of every injury"?

Such specious reasoning, by appearing on the surface reasonable, insidiously undermines one's actual understanding of the condition which he is treating. It is easy to see how the habit of treating these injuries by "feel" rather than by diagnosis becomes fixed. If you are called on to examine a knee injury and you respond by saying "pack in ice until morning," the next time the trainer or coach has to manage this injury he will "pack it in ice" himself. Indeed, if the treatment is to be standardized into such a pattern, he is perfectly correct to do so.

It has been shown through years of observation, however, that nonsurgical treatment is not always the best treatment. Among orthopedists there may be considerable difference of opinion as to just how often surgery is indicated and just how complete the surgery should be. But I know of no one, particularly one interested in the treatment of knee injuries, who would say that surgery is never indicated. It must be admitted, therefore, that surgery is indicated for certain types of injuries.

An objective study of results shows that surgery done early, within 10 to 14 days, is distinctly more favorable than surgery done at a later time.[1b] Careful investigation of many cases has shown that the most vital single factor governing the degree of recovery from a severe knee ligament injury is not the severity of the injury, the location of the tear, or the age of the patient; it is the time at which the operation is done.[1b] Almost without exception in this long series (over 100 cases), the patient who was operated on within two weeks obtained a better end-result than a comparable patient operated on at a later time or treated nonsurgically. The patient with a mild injury, for whom indecision and procrastination resulted in considerable delay before operation was done, obtained a much less perfect result than did the patient with a severe injury, for whom operation was done promptly. The very nature of the most severe injuries made decision to operate easy, and the operation was carried out immediately. These patients, in spite of the major injury, obtained excellent results, much better results than those obtained by patients who were less severely hurt, for whom the operative indication was not so clear and surgery was postponed or not carried out at all.

If we are prepared to concede, first, that there will be some cases in which surgery will be indicated and, second, that surgery is much more successful if done early, it must follow that the decision as to whether a patient is to be given surgical treatment must be based on early, thorough, careful examination, with the patient under anesthesia if necessary. All knee injuries must not be treated alike if the best results are to be obtained. Therefore, diagnostic procedures must be an integral part of any discussion of surgical treatment of ligament injuries.

The fact that a high proportion of these injuries occur in young athletes serves to emphasize the importance of the above statement. The athlete must have 100% recovery, or he is no longer an athlete. The athlete demands your best effort in order to preserve his athletic ability. By the same token, every patient should have this same major effort to restore him to normal.

The following precepts are a guide in the management of knee ligament injuries:

First, the goal must be complete recovery. Experience with many cases has emphasized the importance of this concept. If the immediate decision is that recovery cannot be complete and is not even worth attempting, it is obvious that it will not be complete. If we do not aim for 100% recovery, we certainly will not attain it.

Second, avoid expediency. Particularly in the athlete there are great pressures applied to avoid comprehensive treatment. The player is anxious to return to play, and the pressures of relatives and coaches that he continue competition are real. However, in the final analysis, a temporizing attitude satisfies no one. It is important that the physician decide what treatment should be done in a given case, then see that it is done.

Third, the best treatment rather than the most convenient must be selected. It must be important to the doctor to restore the patient's activity to the level he had before he was injured. If the patient wants to play football, this desire should be considered as an important one and not casually shrugged off. Once he realizes this, the player will cooperate fully with your recommendations. Bear in mind that his career is as important to him as yours is to you. Would you willingly give up your career in medicine if this could be avoided by more careful management? It is no more fair to expect him to give up his.

Fourth, treatment must be prompt. A definite decision as to proper treatment must be made at the earliest possible moment. Surgery must not be reserved for those cases where other methods have failed. Surgical treatment is a method to be chosen on its own merits and not backed into by failure of other methods.

Anatomy

The knee joint has no basic stability inherent in its bony structure. It has neither the ball and socket of the hip nor the mortise and tendon of the ankle. The slight bony stability that exists is due to the fact that the lower end of the femur is a bipod and

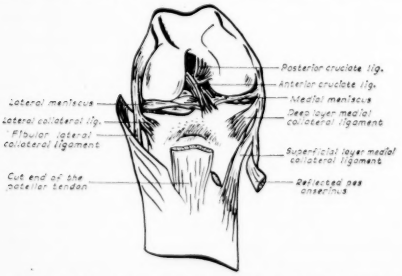

Fig. 1.—Front view of knee with thigh flexed at 90 degrees. Note two layers of medial collateral ligament. Note also that medial meniscus is firmly attached to it.

so resists lateral motion without actual separation of one or the other condyle from the corresponding articular surface of the tibia (fig. 1 and 2). Essentially this stability is obtained by the complete investiture of ligaments which surrounds the joint and prevents separation of the femoral condyle from the tibial plateau. The medial and lateral collateral ligaments which become continuous with the posterior ligament behind and the patellar retinaculum in front serve to give this added stability. The posterior ligament which is tight only in complete

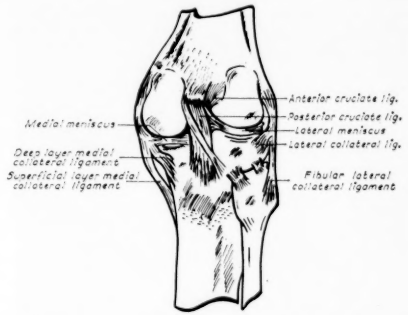

Fig. 2.—Posterior view of knee in 180 degrees extension. Note that lateral meniscus is not attached to lateral ligament and that posterior cruciate is tight in extension.

extension prevents hyperextension of the knee and supports lateral stability when the knee is in complete extension. In order to permit flexion of the knee, the anterior ligament is attached to the quadriceps' mechanism, which permits motion under constant tension. The thickening of the ligamentous structures which make up the medial and lateral collaterals serves to give lateral stability. The anterior and posterior cruciates prevent anteroposterior displacement of the tibia on the femur. Each of these ligaments has its essential function and the function of each is supplemented by the other ligaments. The integrity of the knee is entirely due to the ligamentous support which it receives. Hence a ligament injury is doubly significant in the knee since the osseous portion of the joint does have so little inherent stability.

The cause of a sprain is an abnormal motion of the joint which throws a stress on the ligament designed to prevent this motion. Forcing motion beyond its normal limit will result in some degree of injury to the ligament primarily involved. In the knee joint, this motion may be in any direction; adduction or abduction, overextension, internal or external rotation, forward or backward displacement, or almost any combination of these, although certain particular combinations are much more frequent. Much depends on an accurate diagnosis of the nature of the injury. Knowing the manner of injury certainly can give a lead as to the type of ligament damage to be expected. In one classic injury, the foot is fixed to the ground, the thigh rotates inward and the leg outward; the knee is forced inward toward the opposite leg and the

stress is primarily received on the ligaments on the inner side of the knee (fig. 3 and 4). This is by far the most common type of the athletic injury of the knee. Using this type as an example, what may we expect in the way of injury, provided it is known

Fig. 3.—Note force applied to lateral side of knee. Cleats are fixed to ground, leg is forced into external rotation and abduction; knee opens up on medial side and tibia is forced forward in relation to femur, tension being placed on medial collateral and anterior cruciate ligaments.

that this accident occurred by the familiar lateral blocking (fig. 3) or by the "cut back" motion of the running athlete? As the foot is forced into external rotation, stress comes against the medial collateral ligament of the knee, the superficial layer of which takes the strain first. As this stretches, tears, or gives way, the force reaches the deep layer, to which is attached the medial meniscus. If the force continues, the anterior cruciate receives the stress and it too may give way, and in severe injuries the posterior cruciate may also rupture. These injuries are shown in the accompanying illustrations. Obviously, the injury may stop at any point in this progression of events. In a similar manner, adduction or internal rotation puts the force against the lateral ligament of the knee, the lateral cartilage, and the anterior and posterior cruciate. So also hyperextension at the knee throws initial stress on the posterior ligament of the joint, followed by stress against the posterior cruciate ligament and the cartilages. Direct forward motion of the tibia on the femur will injure the anterior cruciate, while the opposite force will damage the posterior cruciate.

Diagnosis

To consider the diagnosis of injury to the joint, what are the important factors? First a general evaluation of the situation: Did it seem to be a serious injury? Was the player immediately disabled, or was he able to keep going? Did he feel that he had a serious injury? Was he able to come off the field under his own power, or was he carried? Was he suffering extreme pain, or was it relatively mild? After this evaluation, an early, careful, and complete physical examination of the joint is of major importance. The earlier this can be done the better, since often elements can be noted early which become obscure after pain and swelling screen the symptoms. Note whether tenderness is at the joint line, above the joint, or below. Check the knee carefully for abnormal mobility in all directions, including rotation, lateral motion, and anterior and posterior motion. Observe the degree and rapidity of the swelling. Investigate whether the knee was actually locked at the time of injury or whether it is actually locked at the time of the

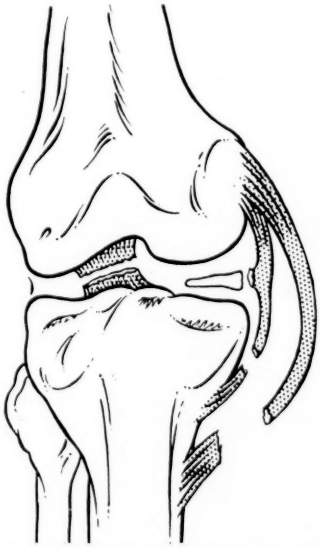

Fig. 4.—Classic injury resulting from forces shown in figure 3. Note superficial layer and deep layer of medial collateral ligament torn near tibial attachment. Medial meniscus is ruptured and anterior cruciate ligament has torn completely.

examination. All of these things are of extreme importance if they are done in the early stage before pain, swelling, and apprehension become factors. Often, in this initial examination, a definitive diagnosis as to the location and extent of ligament injury can be made.

The injury must be classified as to severity as well as location. The simplest classification of knee ligament injuries is into three divisions: mild, moderate, and severe.

Mild Injury.—In a mild ligament injury, we postulate that there has been some damage in the ligament but that its strength has not been materially impaired. The symptoms of such an injury are tenderness at the site of the tear; pain on active use of the knee; local swelling at the site of the injury; pain on forced motion or attempt to duplicate the motion which caused the damage. The negative findings which are important in diagnosis of a mild injury would be no instability, no blood in the joint, no effusion in the joint, no locking of the joint, and no pain on ordinary motion of the joint.

Provided that determination can be made that it is a mild injury, treatment can be based on the premise that the ligament is actually intact. This type of ligament injury where prolonged and extensive treatment is not necessary fortunately includes the great bulk of ligament injuries. The basis of treatment is (*a*) protection against further injury and (*b*) relief of local symptoms by injection into the involved ligament some of the various substances such as procaine, hyaluronidase, or hydrocortisone. With this injury, activity can be resumed at once or at least relatively soon, but active sports should not be permitted immediately after local anesthesia. Complete immobilization is neither necessary nor desirable. The patient may be rapidly rehabilitated without danger.

Moderate Injury.—In the second group, the moderate ligament injuries, it is considered that the ligament has been partially torn, rather than just having had a few fibers of the ligament pulled apart or separated. A certain definite portion of the ligament has been damaged and its strength impaired. It may be 10 to 90% ruptured. The symptoms here are similar to those of the mild injury only greater in degree. Each of these groups shades imperceptibly into the other. The positive findings are pain in the knee; tenderness at the site of the injury; disability of a greater degree than in the mild type; swelling at first localized at the area of damage, followed by swelling diffusely about the joint; fluid or blood in the joint; pain or reproduction of the force and direction of the injury; and possibly locking due to cartilage damage. There is no abnormal motion either laterally or in anteroposterior displacement of tibia on femur. Findings indicating complete avulsion of a ligament should not be present if the damage to the ligament is only partial.

The treatment of moderate sprain is based on the premise that there has actually been significant damage to the ligament with weakening of its structure and considerable loss, or at least potential loss, of function. Therefore, it must be more comprehensive than in the mild group. Treatment consists of rest, local injection, compression bandage, cold pack early, followed by heat, later protection by splints, pressure dressing, and aspiration of the joint. This must be followed by a period of rehabilitation, the rehabilitation being necessary since there is a required period of immobilization during the course of treatment. In rehabilitation, active physical therapy, increasing active use, protective strapping, and reeducation are all of considerable importance. This group of ligament injuries is the one where injudicious overuse or too early return to physical activity may make the difference as to whether or not recovery is prompt and complete. Reduction of pain and swelling by local injection must not be permitted to cover up the true nature of the injury since active stress must not be allowed until healing is complete. Ordinarily recovery should be expected, with no residual disability in the joint. By far the major number of knee ligament injuries will fall in the first and second groups.

Severe Injuries.—In consideration of the third group, the severe ligament injuries, diagnosis is based on the premise that one or more of the major ligaments of the knee is completely torn loose from its attachment, or torn through its substance. The mechanism of this injury is that previously mentioned, namely, forcing the knee through a wide range of abnormal motion beyond the tolerance of the ligament. The symptoms in this type of injury are much more severe. Examination and evaluation reveal immediate disability; giving away of the knee joint; severe pain in the knee and leg; definite abnormal motion (may be rotatory, lateral, or anteroposterior); instability of the knee joint; blood in the joint; blood infiltrating through the tissues; local swelling first at the site of injury and very rapidly into the knee itself; locking, which may or may not be present; and confirmatory x-rays showing abnormal lateral motion at the knee joint (fig. 5).

The treatment of this serious type of ligament injury is extremely important and this is the field where there has been some difference of opinion as to the best measures to be employed. Fortunately, this type of injury is not common, but, when it does happen, it can be disabling to the point where the athletic career is abruptly terminated.

If at all possible the diagnosis must be made at once. If one waits three or four weeks until swelling and pain subside instability becomes quite obvious. The optimum time for treatment has passed. Diagnosis must be early and definitive in order to permit the proper decision as to treatment.

Once the diagnosis of a complete ligament tear has been made the method of treatment must be elected. It will not suffice to try so-called conservative treatment first and then proceed to surgery. Early repair yields so much better and surer results than late repair or reconstruction that surgery must not be reserved for those cases in which conservative treatment has failed. Modern anesthesia, operating room asepsis, highly skilled personnel, and antibiotics have minimized the hazards to the degree that in the well-run hospital with a competent surgical team, open surgery can confidently take its place alongside nonsurgical measures. In the absence of complicating factors the management chosen must be that method which will give the highest percentage of the most complete recovery and in the shortest time.

I believe that if one can demonstrate complete severance of any single ligament or of any combination of ligaments of the knee surgical repair of that unit without disaster, the very fact that the cruciate is one of those factors means that the knee is actually or potentially less than normal without it. The cruciate should be repaired since in no other way may a normal knee joint be attained.

I examine many knees in which the only detectable complaint is cruciate instability. These patients seek treatment because to them the condition is materially disabling. This in itself is evidence that the cruciate in a given case may be vital for adequate function.

Late cruciate reconstruction is highly speculative and should be done only when the stakes are high, as, for example, a professional baseball player who is unable to play because of anteroposterior instability. Early cruciate repair is highly successful and should be done as a matter of course. It is not unduly technical and any competent orthopedist can do it if he properly prepares himself in the necessary technique.

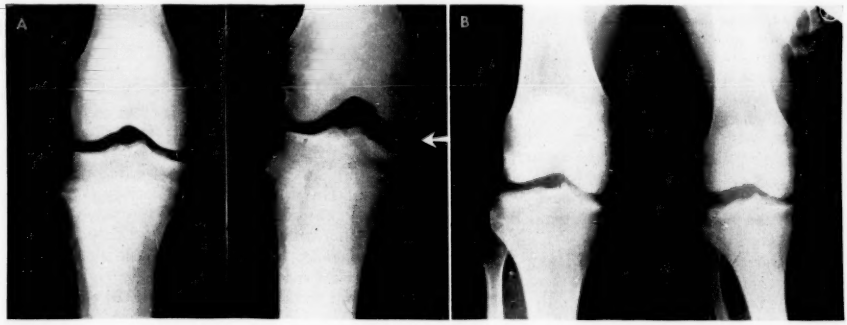

Fig. 5.—*A*, x-ray of injury to medial collateral ligament of knee: *left*, normal anteroposterior view; *right*, position of abduction of leg on thigh; arrow indicates increased tibio-femoral point space. *B*, x-ray illustrating damage to lateral collateral ligament: *left*, straight anteroposterior view of knee; *right*, with leg adducted on thigh.

is mandatory. The repair should include not only one ligament but all ligaments involved. It makes little sense to go to the trouble of repairing the collateral ligament and ignore the cruciate because it "adds to the severity of the operation" or is "too difficult" or "may not be essential." The cruciates are not vestigial. One has only to examine the splendid mechanism of the anterior cruciate, to note its size, to check its strength, and to recognize its vital structure in order to realize that this is not an evolutionary misfit ready for the discard. The cruciates play a living vibrant part in that ingenious mechanism that is the knee. We may argue about their exact function but be assured they have a major one.

Even though we agree that the knee has many interlocking ligaments and that it acts as a physiological unit and that it may spare some portion

In certain cases the ligament may repair spontaneously, especially the collateral ligaments. The danger is in our inability to determine short of surgery which case will heal with normal length and which will not. I have actually found at surgery the tibial end of the medial collateral lying in the joint on top of the medial meniscus (fig. 6). I have seen the ligament torn with the ends free and the tendon retracted an inch or more (fig. 7). I have located the femoral attachment of the medial collateral ligament lying in the joint on top of the meniscus (fig. 8) with the femoral end of the posterior cruciate lying over the medial meniscus. There are many other such situations which are unredeemable except by surgery. With such pathology actually seen, one becomes very skeptical of uniformly good results reported from nonsurgical treatment.

What about results of surgery? After a survey [1b] of 80 consecutive cases of ligament injuries the findings showed that, regardless of the severity of the injury, early repair gave approximately 90% of good results (over 90% in athletes). The time and

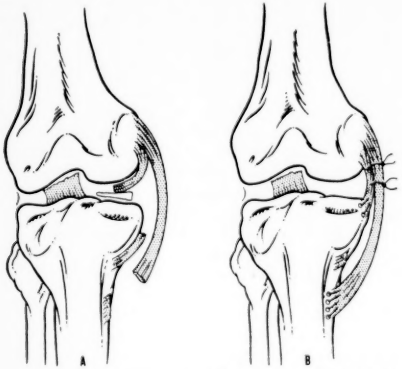

Fig. 6.—Injury from rotation-abduction force, before (*A*) and after (*B*) repair. Note deep layer of medial collateral ligament torn from tibial rim and from cartilage and lying on top of cartilage, requiring surgery for deep layer to be repaired. Note femoral attachment of anterior cruciate avulsed and widely separated.

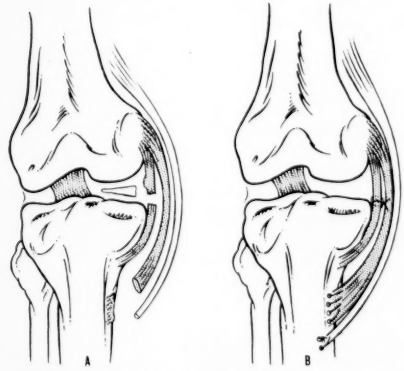

Fig. 7.—Classic injury of semitendinosus tendon attachment pulled loose, with wide separation of ligament attachment, before (*A*) and after (*B*) repair.

the completeness of repair were much more important than the nature or severity of the injury. Failure of the cruciate repair was the biggest single cause of permanent disability in knee ligament injuries. Repair of the cruciate was highly successful early but very unpredictable late.

Bennett [2] lists four musts for the surgical treatment of knee ligament injuries: 1. The patient must be seen early. 2. The surgeon must be a good diagnostician and able to identify ligament injuries. 3. The surgeon must have good judgment. 4. The surgeon must be competent. Certainly these are not unattainable goals for the present-day well-trained orthopedist.

Management of Severe Ligament Injury

Let us consider the actual management of a severe ligament injury. In diagnosis, much depends on patient cooperation, so gentle hands are an asset indeed. Usually one finds immediate disability, often severe, knee "giving away," severe pain, blood infiltration with or without blood in the joint, "doughy" swelling, tenderness, diffuse with local

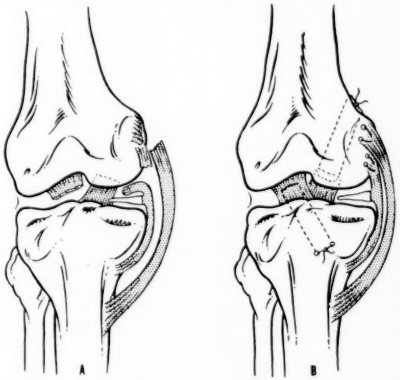

Fig. 8.—External rotation-abduction injury, before (*A*) and after (*B*) repair. Note tibial attachment of anterior cruciate torn loose and separated; femoral attachment of posterior cruciate pulled away; both layers of medial collateral ligament torn away from femoral condyle; deep layer folding inward and lying on top of cartilage. Note anterior cruciate was fastened to tibia, posterior cruciate fastened to femur. Medial collateral was pulled away from joint and attached to femur.

areas of increased tenderness corresponding to the location of the tear or tears. Above all, one finds instability corresponding to the ligament involved. In order to determine this instability the good knee is examined first and a base obtained. Each motion in the injured knee is carefully compared with that of its fellow. The knee is checked in complete extension for adduction and abduction; then flexed to 150 degrees and abduction, adduction, and internal and external rotation are tested; then flexed to 90 degrees so the drawer sign cannot be elicited.

Twenty-five per cent of my cases of cruciate severance were not definitely diagnosed before anesthesia.[1b] After this careful examination, decision is made as to the treatment. If one can demonstrate complete severance of any ligament, surgery is advised. The exact details of surgery for repair of various ligaments to the knee have been thoroughly described elsewhere and need not be repeated here. The thing with which I am vitally concerned in this discussion is the indication for surgery, not the technique. After surgery, a heavy posterior long leg plaster splint is applied, care being taken to support the extremity by the foot and thigh, rather than beneath the calf, in order to avoid stress on the anterior cruciate ligament due to lifting the tibia forward on the femur. After this first splint has set a lateral stirrup is applied.

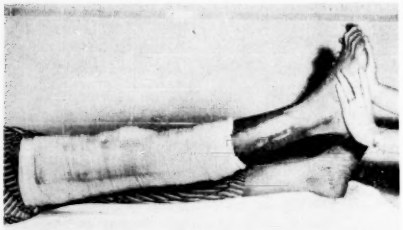

Fig. 9.—Completed cotton cast, splint being pressure bandage consisting of multiple layers of sheet wadding followed by yucca board for stability. See Campbell's "Operative Orthopedics" (edited by J. S. Speed, ed. 3, St. Louis, C. V. Mosby Company, 1956, vol. 1, p. 88) for complete details.

After the patient has returned to bed, the leg is elevated on pillows or a sling and carefully watched for circulatory impairment. The dressing is split before tightness becomes a problem and tightened up as the swelling subsides. At two weeks, this splint is carefully removed and again care is taken in the case of the anterior cruciate repair to support the extremity by the thigh and foot and not by the calf. Stitches are removed. The knee may be aspirated and hydrocortisone (Hydrocortone) or prednisolone (Hydeltra) injected if indicated by the presence of the effusion. This is not ordinarily necessary.

A very light weight long leg plaster cast is then applied with the knee fixed at 160 degrees. Frequently a walking heel is used if the repair seems stable and the patient is reasonably agile. He may use the heel for weight-bearing but is advised to continue use of crutches. At the end of two weeks in the solid cast, four weeks postoperatively, this cast is removed and a cotton cast (yucca boards over sheet wadding) applied (fig. 9). Aspiration and injection are repeated if indicated. This splint is removed in two weeks (six weeks postoperatively) and an elastic bandage utilized as indicated. If effusion persists, repeated aspirations and injection may be necessary. This is not usually necessary. Most cases do not require even one aspiration.

For rehabilitation, quadriceps setting and straight leg raising of both legs are encouraged from the first day. Patient is in a wheel chair 24 to 48 hours postoperatively. He should be able to raise the leg actively, splint and all, by 48 hours, and to walk on crutches in three to five days. Weight-bearing is not permitted, however. After the solid cast is applied (two weeks postoperatively) the patient may walk with crutches on a walking heel if progress is good. He is permitted to discard his crutches if he feels able to walk around the house without them, but in general he should use his crutches while away from home. Meantime exercise of all other available muscles is encouraged.

After he goes into the cotton cast (four weeks postoperatively), he is urged to walk, preferably without his crutches, and to continue his exercises. At six weeks the cotton cast is removed and quadriceps rehabilitation begins in earnest (see table) and continues until the circumference of both thighs is equal. Specific written instructions with definite exercises are important. The actual level of activity varies much with the individual patient. The agile, wiry type of person, relatively light weight, may be allowed more freedom than the heavy lumbering giant whose ligaments are normally relaxed in all his joints. Running is permitted as desired if synovitis permits. No contact sport is allowed until four months, and not then if the quadriceps is not completely rehabilitated.

Rehabilitative Exercises to the Quadriceps Muscle After Knee Injury or Operation

Sit on the side of the table with the legs hanging over in a vertical position.

Raise the foot on the involved side to the horizontal position slowly to the count of 3 seconds.

Hold in horizontal position to the count of 3 seconds.

Lower slowly to the count of 3 seconds.

Rest for the count of 3 seconds.

Repeat this 10 times. Rest a little.

Do this through 3 series of 10 times each, i.e., 30 times total.

These exercises should be repeated two or three times a day depending on tolerance.

When able to complete the series of 30 elevations, add weight to the foot at the next period of exercise increasing its use until it can be used the full 30 times.

Continue these exercises, adding weight successively according to tolerance until possible to raise 25 or 30 lb. through this series. Use opposite knee for control to get some idea of how much weight injured leg should be expected to raise.

Make a chart for daily progress and record on it each period of treatment, noting the ascending curve of weight-lifting capacity.

Continue exercises until circumference of involved thigh is same as uninjured thigh and until injured leg is able to raise as much weight as uninvolved side. As strength increases, these exercises can be supplemented by other exercises, such as going up and down stairs, partial knee bends, single knee bends.

Naturally, each case must be strictly individualized both as to type of repair used and as to postoperative management. A patient with a good tight repair with strong ligament fibers can be permitted more liberty. Some patients need to be pushed in their rehabilitation (for example compensation cases and females). Other cases must be held down (for example 16 to 18-year-old athletes). The elastic bandage should be discarded early in the timorous and retained as a reminder in the overbold. If effusion persists, the usual treatment is followed: aspiration, repeated as required with injection of hydrocortisone, and use of elastic bandage as long as effusion is notable.

Such a regimen carefully followed with early examination, prompt decision, and complete repair of all torn ligaments, followed by conscientious rehabilitation, will give increasingly gratifying results in treatment of major injuries to the ligaments of the knee.

In my series of over 150 cases, 80% were under 25 years of age and 55% under 20 years of age. Since so many of these cases occur in young people, one must be particularly on the alert to try to reach the goal of the best recovery of function in the shortest time.

Lee at 10th Street (3).

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2. Bennett, G., in O'Donoghue.[1b]

MANAGEMENT OF ANKLE INJURIES SUSTAINED IN SPORTS

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Inexact diagnosis and inappropriate treatment of ankle injuries can lead to serious disability. Decisions regarding them should be left to a physician whose authority should not be questioned. The patterns of fracture of the malleoli as seen in anteroposterior roentgenograms can give valuable information about concomitant rupture or avulsion of ligaments. If advantage is taken of the 20 to 30 minutes after injury before edema, hemorrhage, and spasm occur, closed reduction of even grossly displaced fractures can sometimes be accomplished with almost no discomfort. If roentgenograms indicate that soft tissues are ruptured or trapped between bony parts, prompt surgical correction is indicated. Cold, compression, rest, and elevation are the four basic elements of treatment for minor injuries. There is no justification for the use of procaine as an immediate therapeutic agent in any athletic injury. Operation was necessary in the case here described, but active motion without weight-bearing was started at 3 weeks, weight-bearing was permitted at 15 weeks, and skiing was resumed at 18 weeks after the injury.

The doctor who assumes responsibility for a group of athletes is in a unique position to study trauma. Circumstances are ideal for observation of injury from the moment of occurrence to full recovery. In sports involving quick pivoting on a fixed foot, such as football, soccer, and basketball, or unanticipated wrenching with a lever as in skiing, a high proportion of these injuries will involve the ankle.

The incidence of injury can, of course, be reduced by physical conditioning and the acquisition of skill in the techniques of the sport. It is a truism that the outstanding athlete is rarely injured, and then only under unusual circumstances. But not all participants in active sports are neuromusculoskeletal geniuses, nor do they have the time to become technical virtuosos.

For these, a considerable measure of protection is afforded by regular use of ankle wraps.[1] Applied over the inner of two pairs of socks, with a turn around the heel (fig. 1), these nonelastic bindings, which the player applies himself, effectively limit lateral mobility without interfering with flexion or

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extension. When required of all players at all practice sessions and games, the incidence of ankle injuries can be reduced at least 50%.[2]

Despite conditioning, ankle wraps, and skillful coaching, ankle injuries still occur, and the doctor's duty begins at the moment of injury. He should himself go on the playing field and decide whether the injured player should continue play or leave the game, and, if he leaves, whether he should walk or be carried. To leave such decisions to a coach or trainer is to gamble with future disability with the cards stacked against the player. The doctor's authority in these and other medical matters should be absolute and unquestioned. Practically

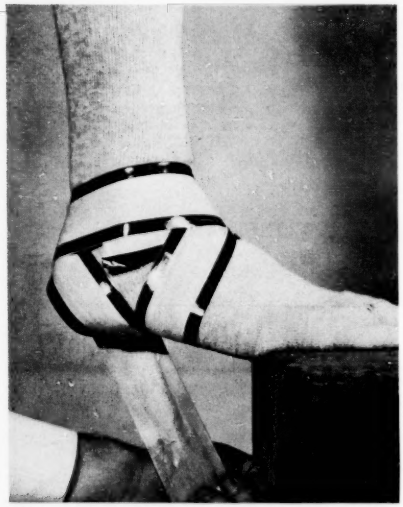

Fig. 1.—Nonelastic protective ankle wrap in process of application. Edges of wrap have been darkened to show basic turns of bandage. Turns around heel limit lateral mobility without interfering with flexion and extension.

all coaches today are quite happy to be relieved of this responsibility. They have enough difficult decisions in their own field.

Once off the playing field a preliminary survey can be made. All that can be accomplished at this time is differentiation between major and minor injury. Minor injury means sprain or incomplete rupture of ligament; major injury means fracture, complete rupture of ligament, or both. Almost invariably, anteroposterior and lateral x-rays will be necessary. Even the most experienced examiner cannot be certain of the presence or absence of fracture or widened joint mortise by examination alone. It is better to take 50 negative x-rays than to miss one serious injury.

Accumulated evidence from observation of the mechanism of the injury as it occurred, the location of pain, tenderness, and swelling on examination, the type of fracture, and the state of the joint mortise from the x-ray should be enough to establish a precise diagnosis of major bone and ligament injury. Fracture is, of course, obvious in the x-ray films, but the diagnosis of complete ligament rupture can be more subtle and, if not recognized, can be at least as serious as fracture in terms of future disability. For practical purposes, only three ligament complexes need be considered: the medial collateral (or deltoid), the tibiofibular-fibulotalar, and the lateral collateral (or fibulocalcaneal).

Most severe ankle injuries sustained in sport are of the abduction–external rotation type, in which the talus twists and pries the fibula from the tibia. Either the fibula itself fractures or the anterior tibiofibular ligament ruptures, producing widening of the tibiofibular syndesmosis (fig. 2). In either event, as force continues, the deltoid ligament gives way (or, more rarely in young men, pieces of the medial malleolus of varying size are avulsed) and the joint space between the talus and the medial malleolus can be seen to be wider than the horizontal component of the ankle joint.

Fracture accompanies ligament rupture more often than not, and the type of fracture, as Lauge-Hansen [3] has pointed out, is a most valuable key to diagnosis. Internal rotation-adduction forces can stretch only the fibular collateral ligament, the others being compressed, and then only if the characteristic horizontal avulsion fracture of the lateral malleolus does not occur (fig. 3). Isolated injuries to this fibulocalcaneal ligament, even when severe, only rarely require primary open surgical repair.

Analysis of ankle injuries sustained in sport should not require much time, and often advantage can be taken of the 20 to 30 minutes after injury, before edema, hemorrhage, and spasm occur, during which nature imposes analgesia, to accomplish closed reduction of even grossly displaced fractures with almost no discomfort.

For external rotation-abduction injuries in which the medial malleolus is intact, the simple device of suspending the stockinette-encased limb has proved most helpful (fig. 4). With the gastrocnemius relaxed by flexion of the knee, the ankle naturally falls into adduction, moderate flexion, and supination, reversing the mechanism of injury. Often little or no manipulation is required to achieve excellent reduction of grossly displaced fracture (fig. 5). Doughnuts of felt or foam rubber are applied over the malleoli and held with sheet wadding before plaster is applied. Most ankle injuries of such severity as to require splinting should be immobilized in a cast extending to the groin with the knee flexed 30-40 degrees.

Another set of x-rays is taken as soon as the plaster has set. If widening of the joint mortise is still present, it can be assumed that avulsed ligament is trapped either between the talus and the medial malleolus, in the tibiofibular syndesmosis, or both and prompt surgical correction is indicated.

Report of a Case

A 25-year-old student sustained a severe external rotation injury to the right ankle while skiing (fig. 6). Closed manipulation without anesthesia and application of a long leg plaster cast was carried out within an hour of injury. Films taken on his return to Boston five days later showed widening of the space between the talus and the medial malleolus and a high fracture of the fibula. At operation, a week after injury, the deltoid ligament was found avulsed from the medial malleolus and trapped in the ankle joint. The anterior and posterior tibiofibular ligaments were completely torn. Clot was removed from the tibiofibular syndesmosis, the deltoid ligament was sutured in proper position, and the tibia and fibula were bolted together. Active motion without weight-bearing was started three weeks after operation. The bolt was removed and weight-bearing permitted three months later. The patient skied again four and one-half months after injury.

Displaced bimalleolar or trimalleolar fractures in young athletes almost always require operation. Precise closed reduction is difficult, since no fixed point remains on which to hinge manipulation, and interposed soft tissue between the fragments of the medial malleolus is the rule rather than the exception. Little less than anatomic perfection can be accepted in these severe multiple ligament and bone injuries since these young men have at least five decades of use of their ankles ahead of them. Only the most trivial fractures, not involving ligaments, can safely be treated by a short leg boot and weight-bearing device.[4] Torsion within a walking boot can displace even the common, and usually uncomplicated, external rotation fracture of

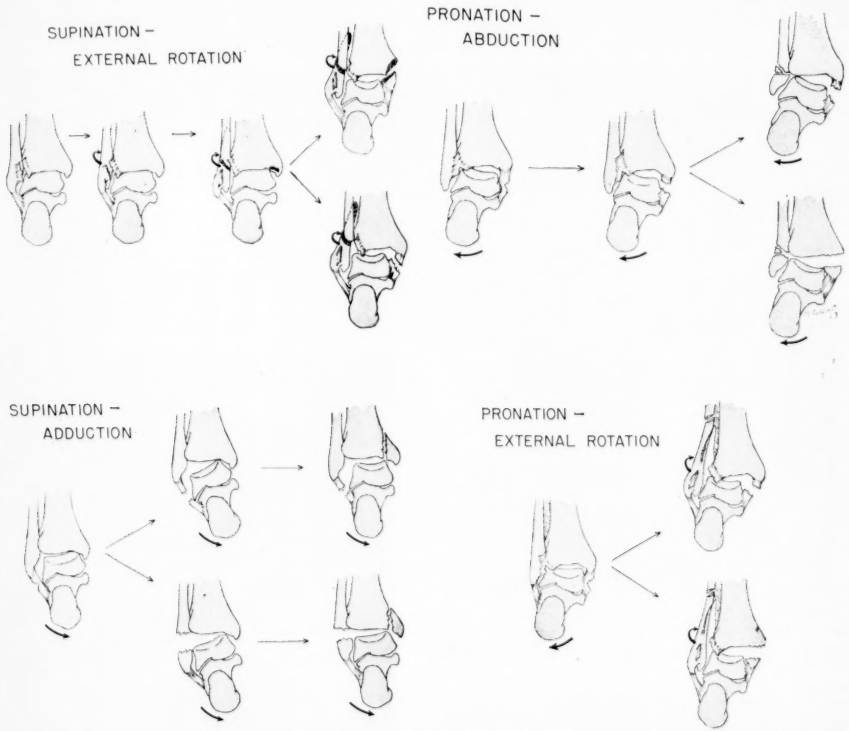

Fig. 2.—Patterns of ankle injury (after Lauge-Hansen[3]). Combinations of forces can occur but are uncommon. Fibula fracture in pronation-external rotation injuries can be in upper half of bone.

the distal fibula, since concomitant injury to the deltoid ligament can be more severe than originally appreciated.

If, at the first examination, within moments of injury, the damage is found to be minor, four principles of treatment are instituted—cold, compression, rest, and elevation. These are based on the concept that a sprain is a partial tear of a ligament, with hemorrhage at the point of tear, absorption of the resulting hematoma, and replacement of the gap by fibroblastic scar. The process

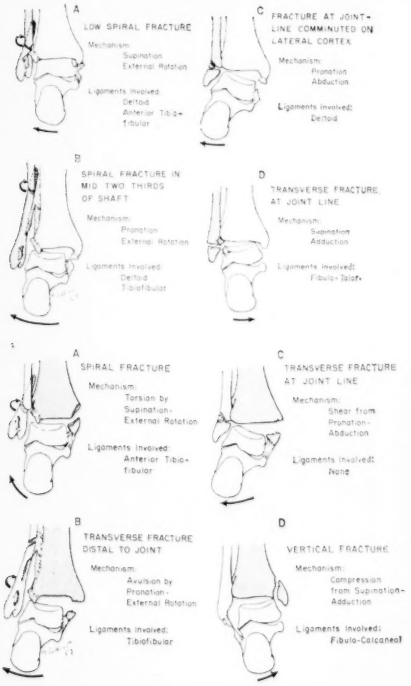

Fig. 3.—Key to analysis of ankle injuries: *top*, fibular; *bottom*, medial malleolar.

is the same as the healing of any sterile wound. No method has yet been found to accelerate the process beyond nature's rate, but many are available which slow it down or disturb the end result. These include the use of procaine hydrochloride (Novocain), hydrocortisone, rough manipulation and massage, and "running it out." Cold, promptly applied, constricts the arteriolar bed and limits the hematoma. Compression disseminates the hematoma already present and speeds its absorption by

Fig. 4.—Stockinette suspension for external rotation-abduction fractures and ligament avulsions. Foot and ankle naturally fall into position which is opposite of forces producing injury. Reduction is often effected without further manipulation.

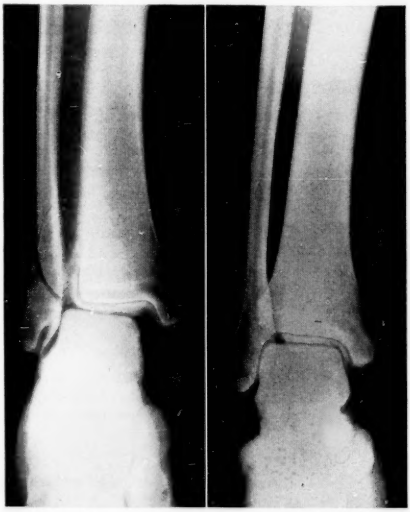

Fig. 5.—Supination-external rotation fracture of fibula with rupture of deltoid ligament before and after 12 hours' suspension in stockinette (fig. 4). Medial side of ankle was explored. Deltoid ligament was found avulsed from its distal attachment and rolled on itself but not trapped in joint.

increasing its surface area (fig. 7). Rest is obvious. As in any injury, whatever motion hurts is wrong, whatever does not hurt is right. Elevation minimizes the edema of dependency and disuse. At this first examination, when the injury has been determined to be a sprain and not a ligament rupture or fracture, a bevelled doughnut of foam rubber, of the tan open-cell type, 2.0 cm. in thickness, is placed over the injured side of the ankle with the malleolus in the aperture. The skin is protected from direct contact with the rubber by sheet wadding. The rubber is then compressed to about half its thickness with an elastic cotton bandage, extending from the toes to the upper calf. The limb is then immersed in cold water (40 degrees) or packed in ice bags for 30 minutes. The wet dressing is then replaced, crutches are fitted, and the patient is instructed in their use. He is advised to spend as much time as possible during the next 24 hours with the ankle elevated above the level of the heart.

At the second examination, 24 hours after injury, edema should be minimal, ecchymosis may already have appeared at the periphery of the foam rubber pad, and by gentle palpation and manipulation an accurate analysis of the particular ligaments involved and their degree of involvement can be made. It is convenient to grade the severity of sprain from 1 to 4, 1 being the least degree of injury which can be classified as sprain and 4, complete rupture. Such classification is of help in prognosis, a matter of great importance to most athletes and coaches. The majority of sprains fall into grades 2 and 3. Experience during the past 70 years at the Harvard department of athletics has established that the commonest ankle injury, a grade 2 sprain of the anterior tibiofibular and fibulotalar ligaments, treated properly, with full cooperation from the patient-player, will be sufficiently healed in 8.2 days to permit full participation in contact sport. It has become equally clear over these seven decades that any prognosis ventured before the second examination, 24 hours after injury, is almost certain to be wrong.

At this second visit, it can safely be assumed that the sources of bleeding have sealed off and heat therapy, followed by gentle centripetal massage, can be started. Electronic and other complicated sources of heat have little advantage over hot water. Diathermy, in fact, is contraindicated in joint injuries since it tends to produce effusion. The psychological effect of a whirlpool bath is much greater than the massage of moving water and bubbles.

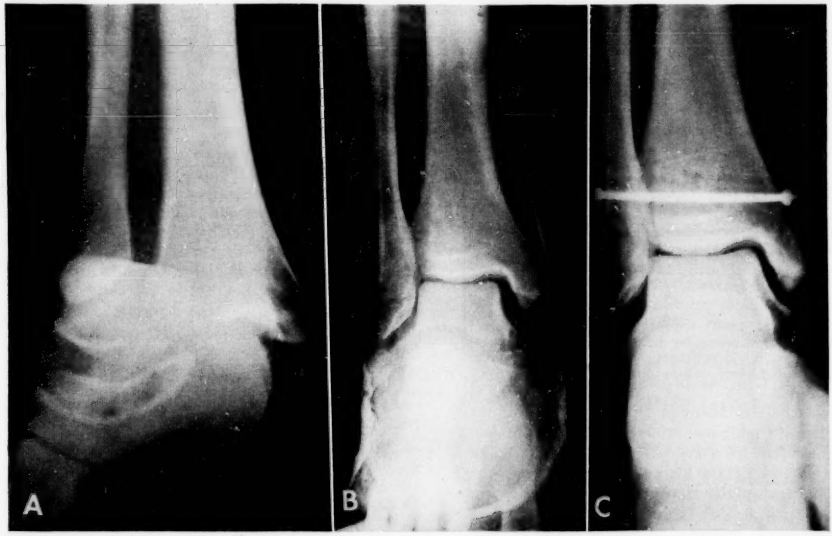

Fig. 6 (reported case).—*A*, film taken immediately after severe external rotation injury sustained in skiing. *B*, film taken five days after immediate closed reduction. Space between talus and medial malleolus is twice as wide as normal. *C*, postoperative film. Trapped deltoid ligament has been removed from joint, and joint mortise has been restored by bolt, which was removed three months later.

Weight-bearing is permitted as soon as natural walking is possible. When pain on manipulation and tenderness approach the vanishing point, the ankle is taped and the player is put through his paces on the playing field under the eye of his doctor, coach, and trainer. He returns to full activity only if his performance is flawless. The ankle

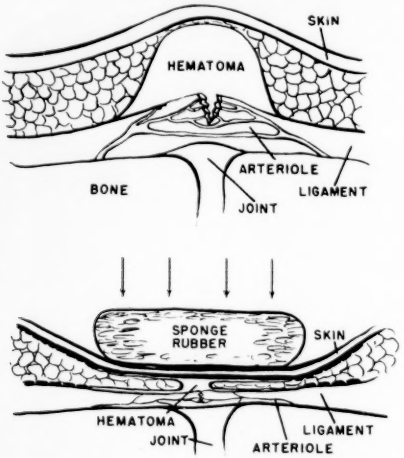

Fig. 7.—Effect of compression on hematoma accompanying a sprain. Blood is disseminated through tissue planes, increasing its surface and speeding absorption.

is protected by adhesive tape, with turns around the heel to minimize lateral mobility for at least the next year for every practice session and game. The old adage "once a sprain, always a sprain" has sound basis in the fact that ligament heals with scar, which is only slowly replaced by orderly elastic collagenous tissue, and the disorganized fibroblast pattern of scar is always weaker than the tissue it replaces.

There is no justification whatever for the use of procaine in any athletic injury. Pain may temporarily be abolished, but performance is usually poor and further damage to the injured structure is almost inevitable. Hyaluronidase and hydrocortisone may have a place when hemorrhage is unusual in degree or sensitivity to pain high. But it must be remembered that arthrocentesis is no different from arthrotomy, from a bacteriological point of view, and a locker room is hardly as safe as an operating theater. Further, no analgesic substance should ever be injected unless it is absolutely clear that pain is much greater than the basic ligament injury usually produces.

Plaster splints are used only for severe or multiple sprains, and are removed as soon as possible. Atrophy of thigh and calf musculature can occur at a remarkable rate and can be corrected only by careful, daily, supervised, progressive resistance exercise.

Summary

A program of management of ankle injuries sustained in sport has been developed over seven decades of experience at the Harvard Department of Athletics and includes methods of prevention, prompt diagnosis, and implementation of treatment for major and minor injuries.

319 Longwood Ave. (15)

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EFFECTS OF IONIZING RADIATIONS ON BENIGN LESIONS.—Irradiation for benign conditions may produce tissue changes more disabling than the original condition for which the x-rays were administered. A latent period of several decades between exposure to irradiation and tissue breakdown is common. Thus, those who administer the irradiation may be unaware of the late consequences. Cancer developed in 22 per cent of the 165 cases reviewed in this study and can be predicted in others. Contrary to previous teaching, carcinoma in irradiated skin of the face is usually of the basal-cell type. The morbidity of this entity is high, but death from radiation necrosis is rare. Surgical therapy should be prompt and thorough. Prophylactic excision may preclude the ultimate development of carcinoma. Evidence gained from this study and those of others suggests that those not fully qualified in the therapeutic use of x-rays be excluded from the application of this potentially dangerous tool.—Bradford Cannon, M.D., J. G. Randolph, M.D., and J. E. Murray, M.D., Malignant Irradiation for Benign Conditions, *The New England Journal of Medicine*, Jan. 29, 1959.

DEGENERATIVE ARTHRITIS OF THE LUMBOSACRAL JOINT

THE END-SPACE LESION

John C. Wilson Jr., M.D., Los Angeles

In 222 patients examined for degenerative arthritis of the vertebral column, the lumbosacral joint was involved in 160 and the other lumbar joints in only 62. A study was made of 125 patients with lumbosacral arthritis. Some had had symptoms as long as 40 years. Only 14 gave histories of real trauma or heavy lifting. Among 11 treated after industrial injuries, roentgenograms showed preexisting lumbosacral arthritis in 10. Usually the acute attack of pain came on during simple movements such as bending forward to wash hands or make a bed. Patients with acute symptoms were treated conservatively with bed rest, anodynes, and physical therapy. They were usually relieved of pain in three to seven days. In the chronic phase the wearing of a brace often gave remarkable relief from pain. Forty-two patients were treated by lumbosacral fusion with varying results; complete relief from pain and recovery of motion was achieved in 18. The major cause of severe low back pain, with or without sciatic radiation, is therefore believed to be degenerative disease of the lumbar vertebral joints, especially the lumbosacral.

From occiput to sacrum there are 134 joints in the bony spine, any one of which may cause pain. This fact is often forgotten when one contemplates the complexity and sometimes resistant nature of pain from intrinsic spinal disease. Because of this complex anatomy, the exact location of lesions which cause pain and the mechanisms of pain itself have been difficult to determine accurately. It is hardly surprising, therefore, that confusion exists among physicians generally as to the etiology of low back pain with or without sciatica.

Historical Review

The literature is filled with conflicting reports. A review of articles written in the past 25 years points out the need for clarification of the common causes of low back pain. The question as to whether deranged lumbar intervertebral joints should be fused or not fused is still a subject of controversial debate.[1] Disagreement among physicians is encouraging, healthy, and, on the whole, to be expected. However, differences of opinion should be based on sound knowledge of existing facts and not on impression or surmise. A study of a subjective complaint such as backache is difficult and fraught with pitfalls. Yet, such studies are necessary so that clinical findings and pathological data can be correlated. Toward this end a review of certain known facts concerning the pathological anatomy of the spine is helpful.

Püschel,[2] in 1930, described the progressive diminution in water content in the intervertebral disk with advancing years. By the end of the 20th year the disk has reached its maximum development; and from this time on changes of a degenerative type become increasingly evident. Mixter and Barr [3] and Naffziger and associates [4] have stressed the importance of posterior herniations of the intervertebral disk in the lower lumbar spine as a cause of low back and sciatic pain. These studies, published in 1934 and 1938, respectively, are significant contributions toward a better understanding of the etiology of pain in the lower spine.

The careful anatomic studies of Harris and Macnab [5] and McRae [6] have demonstrated convincingly the degenerative changes which take place in intervertebral joints with the passage of time. Specifically these changes are disk degeneration, vertebral lipping, and arthritis in the posterior zygoapophyseal articulations. Harris and Macnab [5] have also described these facet lesions in considerable detail. They include loose body and adhesion formation within the joints, synovial and capsular thickening, subluxation, degeneration of articular cartilage, and osteochondral fracture. Emphasis must be placed on the fact that these facet articulations are true joints, and the osteoarthritic changes which occur are no less extensive than those which are seen in synovial joints elsewhere in the body.

The disk itself can be a source of pain, as shown by Hirsch [7] in 1948 and by Lindblom [8] in 1950. However, degeneration of the disk more commonly produces symptoms because of secondary involvement of the facet joints, spinal ligaments, and nerve roots.

While degenerative changes in the vertebral joints must be considered a normal process of aging, premature or accelerated degeneration of one joint or hereditary predisposition to early degeneration of one joint must be considered pathological. Furthermore, degenerative changes in the spine fol-

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low no definite calendar, and the degree and extent to which they occur vary greatly even in individuals of advanced age. Not all degenerative changes are of clinical importance, and, as McRae has pointed out, disks may bulge, herniate, or rupture without any symptoms whatsoever.

This paper is written as a contribution toward a better understanding of degenerative arthritis of the lumbosacral joint. The significance of clinical and roentgen findings to be described will be considered controversial by some. Nonetheless, I feel that a reasonable approach to the treatment of low back pain of intrinsic cause must come from a better understanding of degenerative arthritic lesions which occur in the lower lumbar region of the spine and particularly in the lumbosacral joint.

This joint, the end-space of the movable spine, is a compound articulation which consists of an intervertebral disk and two facet joints. The disk is an amphiarthrosis, a modified joint with a ball-bearing-

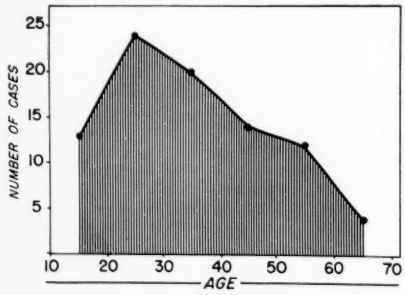

Fig. 1.—Graph showing ages of patients at onset of symptoms of lumbosacral arthritis.

like action. The facet joints are diarthroses or true movable articulations. The first sacral nerve root bears an intimate relation both to the disk and to the facet joints. The lumbosacral joint, subjected to the greatest amount of superincumbent body weight, is more prone to degenerative disease than any other joint in the lumbar spine. In 222 patients examined over the three-year period, 1955 to 1958, degenerative arthritis occurred in the region of L-3 in 5 patients, the region of L-4 in 22, the lumbosacral region in 160, and the region of L-4 and L-5 in 35.

The importance of the lumbosacral joint as a site of degenerative arthritis has been recognized by orthopedists generally, but this concept has been slow to extend beyond the confines of the specialty. Goldthwait,[9] in 1911, described a paraplegia which followed forcible manipulation of the lumbar spine in a 39-year-old man. The patient's signs and symptoms, viewed in light of present-day knowledge, would have indicated a diagnosis of posterior herniation of the lumbosacral disk. The catastrophic result which occurred after forcible manipulation under ether anesthesia caused Dr. Goldthwait to make extensive anatomic studies of the lower lumbar region of the spine. His article, a landmark in the recorded history of orthopedic surgery, is the first to place emphasis upon the lumbosacral joint as the site of disease which can cause pain in the lower back and legs. Prior to his article, and even subsequent to it, the sacroiliac joint, rather than the lumbosacral, has been considered the offending articulation. The concept of sacroiliac displacement as a cause of low back pain is dying a lingering death, but it is far from dead.

Method of Study

One hundred twenty-five patients, of whom 83 are female and 42 are male, were chosen for this study. The patients in the study, and whenever possible their families, were questioned carefully on repeated occasions in an effort to obtain histories of a high degree of accuracy. Special attention was given to the history, for prior to the first examination many had been treated for long periods of time by doctors of varying disciplines. The nature of the treatment that had been rendered and the patient's response to it was carefully recorded. The type, frequency, and duration of acute episodes of pain were charted. Careful differentiation between acute and chronic symptoms has been possible. The progress of the disease has been recorded by careful serial roentgenographic study.

My associates and I have had the unique opportunity of treating siblings and successive generations of the same family with lumbosacral arthritis. The hereditary nature of the disease has become increasingly apparent. Treatment, whether conservative or surgical, has been carried out along certain definite patterns, so that an opinion of some value can be given as to the response of these patients to the care rendered. The majority have been treated conservatively. Some have been followed for as long as 20 years. Clinical data from various age groups have been gathered and sifted. By taking a perspective in length it has been possible to record, in part, the natural history of this disease.

Symptoms in Lumbosacral Arthritis

Of the 125 patients, 87 were aware of the age at which symptoms developed. Most developed symptoms while under the age of 40 (fig. 1). Eighty-four patients were aware of the exact nature of their first symptoms. Twenty-four noted dull ache in the lower back which came on without any known cause. Forty-six had an acute attack of low back pain which resulted from a simple body motion. Fourteen gave histories of real trauma to the lower back which resulted usually from lifting weights in excess of 100 lb.

Eleven patients were treated because of injuries sustained in industrial accidents. It is of interest that roentgenograms taken at the time of injury showed preexisting lumbosacral arthritis in 10 of these patients, and, therefore, their accidents were considered aggravations of an already existing degenerative disease. Included in the study are members of 10 families in whom there was definite evidence of a hereditary tendency toward degeneration of the lumbosacral joint (fig. 2).

The duration of symptoms prior to the initial examination varied from 1 to 40 years. Every conceivable type of treatment had been rendered, including heat of all kinds, medicaments too numerous to record, supports of many types, exercises, traction, and manipulation. It soon became apparent from scrutiny of histories that the type of treatment rendered in the early stages of disk degeneration seems to make little difference. Acute symptoms subsided in a few days regardless of what was done. With respect to manipulative therapy, questioning of the patients indicated that in the first years of their disease such treatment often gave relief. However, as the degenerative

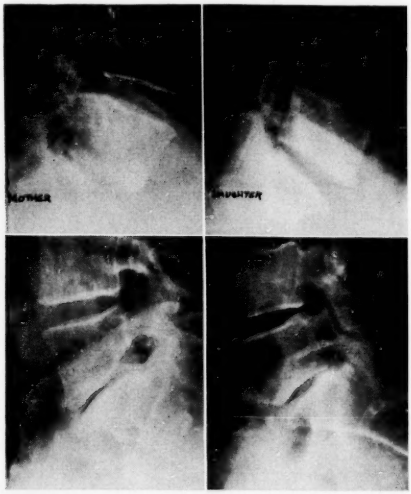

Fig. 2.—*Above*, lateral roentgenograms of lumbosacral joint of woman (*left*) aged 52 and her daughter (*right*) aged 38. *Below*, lateral roentgenograms of lumbosacral joints of two sisters, (*left*) aged 62 and (*right*) aged 56. Note obliteration of joint space.

process of the lumbosacral joint progressed, manipulations either gave no relief or aggravated symptoms.

Patients who ventured a diagnosis at the time of the first examination stated almost invariably that their sacroiliac joints slipped out of place. The frequency of this diagnosis seems to give further evidence of the extent to which this misconception is fixed in the minds of both laymen and physicians alike.

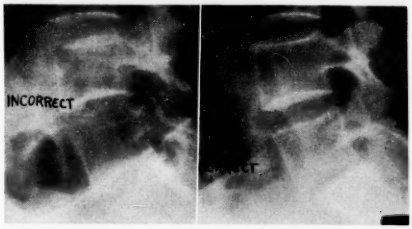

Fig. 3.—Lateral roentgenograms of lumbosacral joint in patient, emphasizing ease with which diagnosis can be missed in poorly centered film and ease with which it can be made in a well-centered film.

Regardless of whether the onset of the disease was acute or chronic, progress of lumbosacral arthritis is characterized by recurrent attacks of low back pain with or without sciatic radiation. These attacks occur at intervals of several weeks to several months. They tend to increase in severity.

Usually the actual attack occurs from a simple body motion such as bending forward to make a bed or to wash one's hands. However, the episode of intense pain is frequently preceded by a period of physical exertion, fatigue, emotional upset, or respiratory infection. The stress of the year-end holidays seems to predispose many patients to an acute attack.

With collapse of the disk space, derangement of the facet joints increases, and chronic symptoms appear. By far the most common of these is stiffness in the lower back on arising from bed in the morning. Some patients are awakened in the early hours of the morning by pain in the lower lumbar region. Others are comfortable until they attempt to arise from bed. The act of assuming the upright posture is painful and difficult. Stiffness and pain may persist for from ½ to 2 hours, but these symptoms gradually lessen with increasing physical activity. Other chronic symptoms include backache with prolonged sitting, pain in the lower back on arising from a sitting posture, backache with prolonged standing, and backache with physical exercise. A housewife with advanced lumbosacral arthritis has great difficulty making a bed, standing to wash dishes, or bending over to use a vacuum cleaner. A businessman finds it painful to sit through a lengthy conference or through a lengthier bridge game. These chronic symptoms are not to be underestimated. They can place se-

vere limitations upon the life of the patient. Constant backache is an irksome burden for anyone to bear.

The location and radiation of pain from the lumbosacral joint is not constant. Inman and Saunders,[9A] in 1944, pointed out that localization of

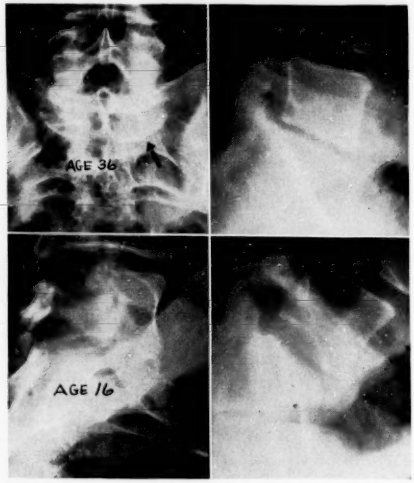

Fig. 4.—*Above*, anteroposterior and lateral roentgenograms of lumbosacral joint in 36-year-old woman. Note symmetrical collapse of disk space, lipping of anterior vertebral margins, and extreme sclerosis of superior articular plate of sacrum. *Below*, roentgenograms of lumbosacral joint of 16-year-old girl who had had symptoms for four years. Note narrowing of disk space in lateral view and loss of joint space as well as subluxation of facet joint in oblique view.

pain from irritation of deeply placed skeletal structures is poor. They further demonstrated the variability in the response of deep structures to painful stimulation. Lumbosacral pain may be felt in the midline of the lower back, over the coccyx, over one or both sacroiliac joints, in the buttocks, in the lower abdominal quadrants, or in the groin. If the first sacral nerve root is irritated, true sciatic pain is felt. Unusual radiation of pain from the lumbosacral joint has led to the unnecessary removal of the coccyx and pelvic organs, especially in the female.

A patient examined in the acute phase of the illness demonstrates marked restriction of motion in the lumbar spine, muscle spasm, tenderness to palpation over the lumbosacral joint, and, depending upon whether the sciatic nerve is irritated or not, hamstring spasm and alteration in the achilles reflex. The signs of nerve root irritation are variable. They may be present with one attack and absent with the next. They bear no direct relationship to the degree of disk disintegration. Patients with total collapse of the lumbosacral disk space have never had leg pain, whereas others with a lesser degree of collapse have had intermittent severe leg pain.

A patient examined in the chronic phase of the disease may show surprisingly little on physical examination. Slight restriction of motion in the lumbar region of the spine and tenderness upon firm palpation of the spinous process of the fifth lumbar vertebra may be the only significant positive findings. A depressed or absent achilles reflex may be a single clue to chronic irritation of the first sacral nerve root.

The diagnosis of lumbosacral arthritis can be strongly suspected from the history and physical findings, but accurate diagnosis depends upon adequate roentgenograms. In view of the slowly progressive nature of the disease, serial x-rays are sometimes needed before the diagnosis is confirmed. Films should include standard anteroposterior and lateral views of the lumbar region of the spine with oblique views and a coned lateral view of the lumbosacral joint. Standing lateral x-rays of the lumbosacral articulation taken with the spine in flexion and extension are also helpful. The importance of accurate centering in the lateral view is especially stressed (fig. 3).

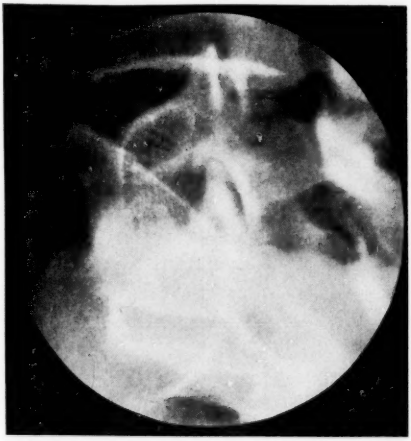

Fig. 5.—Oblique roentgenogram of facet joint at lumbosacral level in 50-year-old woman. Facets are subluxated. Superior sacral facet has impinged on pedicle of fifth lumbar vertebra to such degree that notch has formed in pedicle.

The roentgenographic characteristics of lumbosacral arthritis are demonstrated in figures 4 and 5. The progressive nature of the end-space lesion is well illustrated in figure 6.

If posterior herniation of the disk is suggested by positive neurological findings, a myelogram should be taken, provided the patient is not sensitive to iodine. In my experience, the taking of a myelogram has proved to be a procedure of low risk and high yield. No untoward results have been encountered other than headache. The electromyogram, while occasionally useful, has not proved as valuable a diagnostic aid as the myelogram.

Methods of Treatment

Eighty-three patients have been treated conservatively, and forty-two have been subjected to lumbosacral fusion. Adherence to the principle of rest has guided treatment of the acute attack. Adhesive strapping, suitable anodynes, and confinement to bed have resulted in prompt relief of acute symptoms in three to seven days. Physical therapeutic measures, including luminous heat, deep muscular massage, gentle stretching, and postural exercises, have been beneficial. A firm mattress and a bed board are indispensable. The use of a simple wedge-shaped car seat cushion can make driving for these patients a pleasure instead of an ordeal. Manipulation of any sort has been assiduously avoided.

The therapeutic aid used most frequently, both for the control of chronic symptoms and for postoperative support, has been the Goldthwait back brace (fig. 7). Made of light spring steel and covered in washed kid leather, it is comfortable to wear and is accepted without complaint by the majority of patients. The brace not only relieves chronic symptoms but it enables the patient to engage in light physical exercise without fear of an incapacitating attack of pain. Some patients

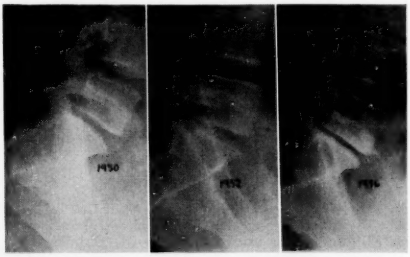

Fig. 6.—Lateral roentgenograms of lumbosacral joint of 43-year-old woman showing progression of disease over six-year period.

in this study have worn a Goldthwait brace intermittently for as long as 20 years with remarkable relief of pain. Both backache and sciatic pain have been relieved through its use. In addition to the use of the brace, patients have been instructed in simple postural exercises. When indicated, weight reduction has been urged.

Of the 42 patients subjected to lumbosacral fusion, 13 had backache alone and 29 had both backache and leg pain. Of those with leg pain, 14 had posterior herniations of the nucleus pulposus. Ten of these were recent and four were older. In the remaining 15 patients, leg pain was found to be due to foraminal encroachment upon the first sacral nerve from collapse of the disk space. Forty-

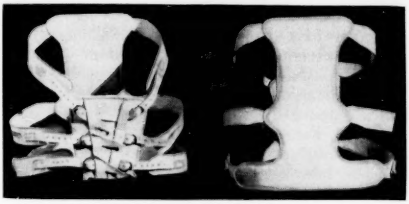

Fig. 7.—Goldthwait back brace.

one patients developed solid bony fusions and one had failure of fusion. The failure occurred in the oldest patient operated on, a woman aged 57 years.

The fusions have been done according to a modified Hibbs technique. Partial denervation of the joint is accomplished by total excision of the ligamenta flava. In addition, the cartilage, synovia, and capsular membranes of the facet joints have been removed. The defect in the facet is filled with bone chips from the adjacent lamina. The laminal arches of the fifth lumbar and first sacral vertebrae have been subjected to erasion, and the fusions have been completed with cancellous bone taken from the posterior superior spine of the ilium. Partial interruption of the nerve supply to the lumbosacral joint,[10] as well as decompression of the first sacral nerve roots, accounts for the improvement which patients note even in the immediate postoperative period.

No support other than adhesive tape and wound dressings has been used during the first 10 days after surgery. Between the 10th and 14th day a Goldthwait brace is fitted, which the patient wears in bed for increasing periods of time. On the 21st day ambulation is begun. The brace is worn night and day for four months and for an additional two months in the daytime only. The integrity of all fusions was tested by bending films taken nine months to one year after operation.

Results

The results in this small series of fusions are as follows: In 18 patients the results are considered excellent. The patients have no symptoms whatsoever and on physical examination demonstrate no limitation of motion in the lumbar region of the spine. Each admits to complete relief of preoperative complaints. Seventeen have had good

results. Their symptoms have been relieved except for occasional mild back or leg ache, usually after exertion. However, they all demonstrate 25% loss of motion in the lumbar region of the spine, particularly in extension and lateral flexion. Two patients have had fair results, for, though fusion occurred, they complain of intermittent back and leg ache. However, both admit to considerable benefit from operation. Two are considered to have poor results. Their lumbosacral joints have fused, but they have many subjective complaints which are not explained by objective findings. One patient has a failure of fusion but is asymptomatic. Two patients have developed degenerative disk disease above the site of fusion. A woman, now aged 52, has a symptomatic lesion at the third lumbar interspace 20 years after surgery. Another woman, now aged 38, has roentgen evidence of an early degenerative lesion at the fourth space which became symptomatic after a severe respiratory infection complicated by paroxysmal coughing. Both of these complications, if they may be so termed, have been treated conservatively with relief of pain to date.

Fusion of the lumbosacral joint has proved to be an excellent procedure, for it has relieved the acute and chronic symptoms of lumbosacral arthritis in 83% of these patients. The operation provides no assurance against further episodes of back ache, for 131 movable joints remain above the area of fusion.

These patients have not all been followed for 20 years. No prophecy is made as to their future complaints. However, taken as a group, their response to operation has been most gratifying, and these operative results are far better than those in patients subjected to so-called disk surgery alone.

Summary and Conclusions

Lumbosacral arthritis is a chronic progressive disease which may be hereditary. Symptoms can appear as early as the second decade of life, but most patients develop backache from this cause in the third or fourth decades. Onset of symptoms may be acute or chronic. While severe attacks occur generally from a simple body motion, they are preceded by fatigue, emotional strain, infection, and occasionally trauma. Although backache is a constant symptom, sciatic pain may or may not be present. There is no definite correlation between collapse of the disk space and irritation of the first sacral nerve root. With progressive loss of disk space and concurrent degeneration of the facet joints, chronic symptoms appear. These may place severe limitations upon the life of the patient and can at times become incapacitating. While conservative treatment of lumbosacral arthritis is often both practical and advisable, spinal fusion in the carefully selected patient relieves the acute and chronic symptoms of the disease.

The author of an essay on backache is likely to find himself making a series of positive statements. There is harm in being always positive, for one may not be always right. The conclusions reached in this paper have not been arrived at hastily. They have been formulated after careful study. The diagnostic criteria and roentgenologic interpretations are founded upon a firm belief that degenerative disease in the lumbar vertebral joints, and especially in the lumbosacral joint, is the major cause of chronic recurrent severe low back pain with or without sciatic radiation. The treatment which has been described, while not the only approach, is reasonable, conservative, and effective.

Morbidity from low back pain is of concern to the general practitioner as well as to the specialist. There is need throughout the profession of medicine for dissemination of knowledge concerning the pathological anatomy of the spine so that the diagnosis and treatment of one of man's most common afflictions will rest upon a firmer scientific basis.

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LATE RESULTS IN OSTEOCHONDROSIS OF CAPITAL EPIPHYSIS OF FEMUR (LEGG-CALVÉ-PERTHES DISEASE)

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and
Richard T. Odell, M.D., St. Louis

In treating osteochondrosis of the capital epiphysis of the femur, it has been difficult to evaluate results and consequently difficult to compare the effectiveness of various methods. There is a need for more reliable measures of hip function and better criteria of results. Of 132 patients in the present series, 34 were treated with bed rest and traction, 31 with crutch and sling, and 25 with crutch and lift; 42 received inadequate treatment or none at all. The percentage of results classified as satisfactory or fair was highest (93%) in the group with bed rest and traction. This group included 10 of the 14 patients with both hips affected. The group inadequately treated had satisfactory or fair results in only 30% of cases. Treatment by means other than bed rest and traction is feasible only if the disease is unilateral and the patient cooperates.

The management of osteochondrosis of the capital epiphysis of the femur (Legg-Calvé-Perthes disease) has been controversial since the original description in 1910.[1] In 1934 Danforth [2] demonstrated the rationale of non-weight-bearing treatment to prevent deformity in the disease. In 1936 Eyre-Brook [3] compared his results of bed rest and traction versus other non-weight-bearing methods of treatment. In 1940 Gill [4] confirmed Eyre-Brook's report, and both claimed essentially normal hips as a result in every case, if therapy with bed rest and traction was begun prior to deformity. In 1951 Pedersen and McCarroll [5] reported the experience at the St. Louis Unit of Shriners Hospital for Crippled Children with bed rest and traction versus ambulatory non-weight-bearing means, and they also concluded that bed rest gave vastly improved results.

Methods

For approximately five years after Pedersen and McCarroll's report, we continued with the bed rest and traction regimen. The crutch and sling replaced the previously used crutch and shoe lift in patients whom we felt would cooperate. Since 1956, only an occasional patient has been admitted to the hospital for a full course of bed rest and traction. At present, traction is used only for a short period to allow the muscle spasm to subside, and then the crutch and sling is recommended. The patients with bilateral cases are still treated by bed rest whether at home or in the hospital. The patients in this series have all been seen at the St. Louis Unit of the Shriners Hospital for Crippled Children. When it was not possible for the patients under study to return to St. Louis for the follow-up examination, we utilized a Shriners hospital in the immediate area or an orthopedic surgeon who would complete the examination. The type of therapy recommended has not been contingent on the financial situation of the family as long as they are eligible for our service. Hospitalization is free, and we have the public school system in the hospital; thus we are not influenced for economic reasons as to which would be the ideal way of managing the patient.

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Read before the Section on Orthopedic Surgery at the 107th Annual Meeting of the American Medical Association, San Francisco, June 24, 1958.

We were interested in ascertaining the outcome of the original patients reported by Pedersen and McCarroll and also in determining whether it is desirable to discontinue the bed rest treatment. Mindell and Sherman [6] could not find a statistical difference between the ambulatory and the non-ambulatory methods, provided the therapy was started early. Heyman and Herndon [7] used a modified program consisting of bed rest until regeneration of the femoral head was noted, 6.3 months on the average, and then followed with a non-weight-bearing brace. They reduced the hospital time without endangering the outcome of the patient.

We have seen 224 patients with osteochondrosis of the capital epiphysis of the femur between 1926 and 1957. The follow-up period has ranged from 5 to 32 years and includes 138 patients. An additional 33 patients have not completed the course of their disease and thus cannot be included in this study.

Evaluation of our results was difficult, and a sincere attempt was made to utilize the comprehensive quotient advocated by Heyman and Herndon. We found that no two observers could measure the adult deformed hip and obtain comparable figures. This difficulty arises when the epiphysis is closed, when the head is slightly or moderately deformed,

and when x-rays are not taken with the hips in similar rotations. We used the epiphysial quotient (fig. 1) as a numerical index in evaluating our cases, and, to reduce the error of variation in measurement, one man did all the calculation. The measurement is taken as the height of the epiphysis

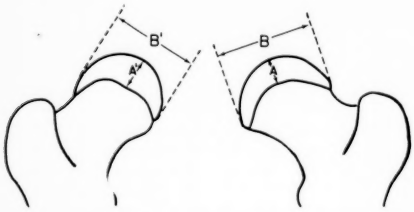

Fig. 1.—Epiphysial quotient described by Herndon but measured by Eyre-Brook's method. *Left*, normal hip. A′=21 mm.; B′=54 mm.; and index 100 A′/B′=39. *Right*, hip affected by osteochondrosis of capital epiphysis of femur (Legg-Calvé-Perthes disease). A=17 mm.; B=61 mm.; and index 100 A/B=28. Epiphysial quotient=28/29=72%.

divided by the greatest width of the head, as described by Eyre-Brook. Herndon used the width of the epiphysis, but this is not possible to measure in the patients with older cases when the line is closed and the head is deformed. The measurement for the normal hip is then divided into that for the diseased hip to determine the apparent percentage of normal. We used 40.7 as the epiphysial index in patients under 15 years old and 37.8 for patients over 15 in determining the epiphysial quotient in the bilateral cases.

Mindell and Sherman utilized a simple and broad classification embracing the clinical and radiographic examinations in a follow-up study of the disease. We have attempted to follow their criteria, and even with this relatively flexible classification some difficulty was encountered. A satisfactory hip (fig. 2) is one that is symptom-free but may have

Results in 132 Patients with Osteochondrosis of the Capital Epiphysis of the Femur (Legg-Calvé-Perthes Disease)

Method of Treatment	Patients, No.	Hips, No.	Results, No.				% of Satisfactory or Fair Results
			Satisfactory	Fair	Poor		
Bed rest and traction	34	44	31	10	3		93
Crutch and sling	31	31	14	7	10		67
Crutch and lift	25	27	5	11	11		59
Inadequate or none	42	44	6	8	30		30

a few degrees of limitation of motion. The x-ray shows the hips to be without deformity. A fair result (fig. 3) has occurred when there are minor complaints, and 1 to 2 cm. of shortening will be noted. X-rays show a moderately flattened and widened femoral head, with or without acetabular changes. Patients with poor results (fig. 4) will have more pain, limp, and have some disability. There will be significant limitation of rotation and abduction. X-rays demonstrated gross deformity of the femoral head and neck and occasionally of the acetabulum.

Results

The 132 patients in our series, with 146 affected hips, have been divided into four groups, according to method of treatment. The results of treatment are shown in the table. The first group was treated with traction, the second with crutch and sling, and the third with crutch and lift. The fourth group is made up of those patients who received no treatment or inadequate treatment or who were seen so late that treatment could not be expected

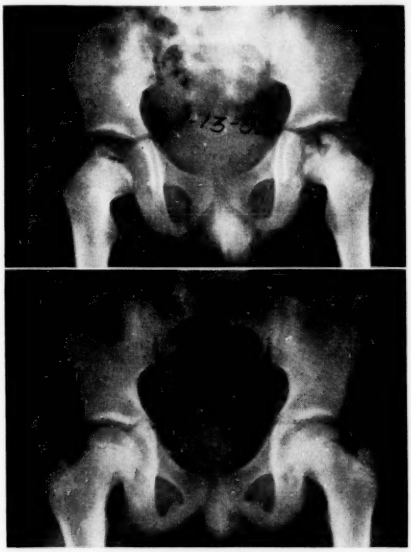

Fig. 2.—*Above*, roentgenogram made when patient was first seen at age 4. *Below*, satisfactory result, with no pain or limp, about six years later.

to reverse the severe deformities already established. Those who were seen early but did not cooperate were retained in one of the three specific treatment groups, as lack of cooperation represents one of the hazards of treatment. Even after reviewing this series of cases, we are still uncertain as to the best method of treatment for patients who are seen late in the course of their disease and with seemingly severe established deformity.

We attempted to correlate these results with the epiphysial quotient and found that in the groups with satisfactory results the hip was 70% or more of normal, the hips in which results were fair varied

between 55% and 70%, and those in which results were poor were under 55% of normal. It was also noted that for 28% of the satisfactory hips the epiphysial quotient was lower than 70%, such as in the example shown in figure 5, which we considered satisfactory but in which the epiphysial quotient was 63. We also found that 25% of the fair results did not fall within the prescribed range and 10% of the poor exceeded 55% of normal.

All of the above patients were followed for at least 5 years and some for as long as 32 years (fig. 6). The average length of follow-up by groups is bed rest and traction, 8 years; crutch and sling, 6.6 years; crutch and lift, 12.2 years; and inadequate treatment, 19.8 years. The average follow-up period for the entire group was 11.8 years. Ninety-five per cent of the patients in this series have been seen during the six months prior to the time of writing for clinical and roentgenographic examination.

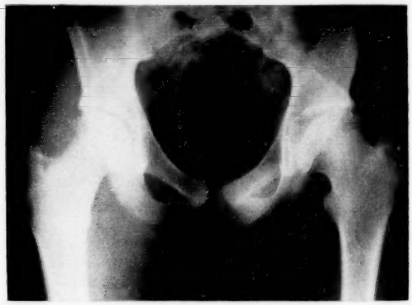

Fig. 3.—Patient treated with crutch and sling for 29 months. Fair results seven years later include no pain, no limp, negative results from Trendelenburg test, 1-in. thigh atrophy, and 0.5 in. shortening.

It is interesting that in the three so-called adequately treated groups, the length of treatment was virtually the same. In the bed rest and traction group, the average length of time this therapy was used was 17.7 months. Unrestricted weight-bearing was not permitted, however, for an additional 11.2 months, for a total treatment time of 28.9 months. Those with the crutch and sling were treated for an average of 27.4 months and those with a crutch and lift for 26.7 months. The additional therapy in the bed rest and traction group was with the use of a crutch and sling. Ten patients in the traction group were allowed unrestricted weight-bearing after traction was discontinued.

We have attempted to analyze the three poor results in two patients in the traction group. One of these two patients had bilateral involvement and was kept in bed for 56 months (fig. 7). Although therapy was begun early in this case, we still are unable to understand why it failed. The other failure was due to our error in permitting too early weight-bearing and demonstrates that even if the hip has started to regenerate flattening can occur.

Six of the 11 patients with poor results in the crutch and lift group were uncooperative, as were 6 of the 10 in the crutch and sling group. Thus,

Fig. 4.—Poor result, after 31 years, in patient, first seen at age 9, with symptoms for two years. He was not adequately followed but supposedly wore an ischiatic weight-bearing brace for eight years.

if we were to remove the uncooperative patients from these latter two groups, the number of those classified as having poor results would be virtually the same in the treated patients.

Perhaps the main advantage of the traction treatment is that we force the patient to cooperate, and the calculated risk one takes in treating this

Fig. 5.—Patient, followed for eight years, with 0.5 in. shortening but no pain and no limp. Result is classed as satisfactory despite epiphysial quotient of 63. Head obviously is flatter than opposite side but if viewed alone would probably be regarded as normal.

disease with the ambulatory non-weight-bearing method is removed. Thirty per cent of the inadequately treated group had a satisfactory or fair result. These were not followed as closely, but 40%

of them may have had sufficient treatment during the vital period to at least slow down their activity and thus achieve a satisfactory or fair result many years later. This 30% did not develop the severe metaphysial changes and appeared to pass through the degenerative and regenerative phases much faster than the average. We cannot state the optimum time for full unprotected weight-bearing, but we agree with Herndon that once regeneration is started increased flattening rarely develops. We prefer to see regeneration of the outline of the femoral head before unrestricted weight-bearing is allowed in the early regenerative phase, lest too early weight-bearing lead to increased flattening of the femoral head.

It is evident from our results that treatment by bed rest and traction will insure the best results in the treatment of this disorder. It is also our contention that a patient with unilateral involvement, who can be followed closely, may be treated with a crutch and sling. Weight-bearing on the degenerating femoral head must be reduced to a minimum to get a satisfactory result. In spite of the fact that bed rest and traction have given a more uniformly satisfactory result in the treatment of this disease, we continue to use the crutch and sling. This seeming paradox arises because there are gradations in severity of this disease and when properly managed the crutch and sling method can insure satisfactory results.

Conclusions

Bed rest and traction (nonambulatory and non-weight-bearing) will insure the best results in the majority of patients with osteochondrosis of the capital epiphysis of the femur (Legg-Calvé-Perthes disease). Therapy with crutch and sling is indicated in cases of unilateral disease where instruction can be given as to the importance of non-weight-bearing methods. Inadequate treatment carries a 70% chance of causing a poor result. Ambulatory non-weight-bearing methods must be replaced with bed rest if the patient is unable to cooperate.

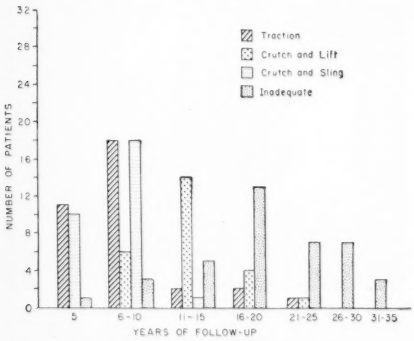

Fig. 6.—Length of follow-up in 132 patients.

600 S. Kingshighway Blvd. (10) (Dr. Stamp).

Fig. 7.—*Above*, 4½-year-old boy with pain in left hip and knee for 12 months; no treatment prior to our examination. Patient was started on bed rest and traction. *Below*, marked limitation of rotation, no pain, cystic area remaining in left femoral head. Result is presently classified as poor but may improve to fair. Epiphysial quotient is 55 on right and 45 on left.

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PATHOLOGY OF JAUNDICE RESULTING FROM INTRAHEPATIC CHOLESTASIS

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Organic disease of the liver can cause cholestasis by mechanical hindrance at any level from the bifurcation of the common hepatic duct to the septal bile ducts within the small portal tracts; moreover, protracted cholestasis from any cause provokes enough inflammatory exudation and connective tissue formation to add a secondary intrahepatic mechanical obstructive component. The more difficult problems in differential diagnosis are presented by cases in which cholestasis occurs without tangible mechanical explanation. Certain drugs, endocrinopathies, and viral infections must then be considered as possible causes. The biliary concrements found in children with the "inspissated bile syndrome" are probably the result rather than the cause of obstructive phenomena. Liver biopsy is sometimes helpful in diagnosis, but at times surgical exploration or percutaneous cholangiography becomes necessary.

Jaundice with impairment of bile flow is said to result either from a disturbance at the site of bile formation, the epithelial cells of the liver, or from interference with the flow in the biliary passages without necessarily being associated with alteration of the liver cells. The mechanism of an obstruction to the bile flow in the extrahepatic bile ducts, for instance, by stones, tumors, or strictures, or jaundice from liver cell injury, appears obvious, and the pathological causes are established. In contrast, interference with the bile flow within the intrahepatic biliary passages is still shrouded in mystery. Although little agreement exists as to both the pathological causes and the mechanism, it might be profitable to review once more the thorny problem which has puzzled clinicians and pathologists since Naunyn's and Hanot's time and which represents one of the main difficulties in the differential diagnosis between "medical" and "surgical" jaundice. It has become more pressing in recent years because therapy with various drugs has produced this type of jaundice with increasing frequency.

Nomenclature

Interference with bile flow in the biliary passages in the liver, as clinically reflected in jaundice with pruritus, and functionally, in elevation of serum alkaline phosphatase activity, and often in total serum cholesterol activity, has been designated by various names. "Intrahepatic biliary obstruction" [1] implies a mechanical obstacle which frequently is not demonstrable. "Cholangiolitis" [2] presupposes an inflammatory process not necessarily present and usually assumed to be in the "cholangioles" by exclusion rather than by actual demonstration. "Periacinose hepatitis" [3] implies a specific localization not found in all cases. It therefore may be advantageous to use the noncommittal term "intrahepatic cholestasis" [4] until the phenomenon is better clarified. Intrahepatic cholestasis, defined functionally rather than structurally, may be the only abnormality present or the predominant one, or it may be just a component of a hepatic disease associated with damage of the liver cells with its functional characteristics.

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Read in the Symposium on Modern Concepts of Intrahepatic Obstructive Jaundice before the Section on Gastroenterology and Proctology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

For any attempt of localization, agreement upon the designation of the anatomic structures is required (fig. 1). The initial biliary radicles lined by the hepatic cell walls thrown into fine microvilli seen under the electron microscope are best designated as bile canaliculi or bile capillaries. They form a chicken-wire-like network separated under normal circumstances from the blood capillaries by half the width of the hepatic cell.[5] They are connected with the bile ducts in the portal tracts by narrow tubes lined by cuboid epithelium with similar microvilli. These tubes, mainly located around the portal tract and far less frequently within the lobule, are best called ductules, although the terms canal of Hering, ampulla, and intermediate pieces (Zwischenstücke) have been applied. The term "cholangioles" creates confusion, since some use it to designate bile canaliculi and others ductules or even the small septal bile ducts.

Intrahepatic Biliary Obstruction

Intrahepatic cholestasis may be produced by mechanical obstruction demonstrable by morphologic means, or it may be apparent only from its

consequences, i. e., bile imbibition without obvious structural causes. Bile pigment is found predominantly in the lobular center in the hepatic cells, usually staining protein coagulums varying in size, in bile plugs in the bile canaliculi, and diffusely staining the cytoplasm of the Kupffer cells. In prolonged jaundice, secondary liver cell injury is indicated by a rarefication of the cytoplasm (feathery degeneration) followed by loss of cells and accumulation of scavenger cells. Bile also accumulates on the lobular periphery, and sometimes proliferated ductules contain microcalculi (fig. 2).

Mechanical obstruction may be located in the larger intrahepatic bile ducts, in the small septal bile ducts within the portal tracts, or in the ductules.

Obstruction at Bifurcation of Common Hepatic Duct.—Occlusion at the forking of the common hepatic duct involves the most proximal point of the main axis of the total bile flow and thus regularly produces jaundice just as lesions of the extra-

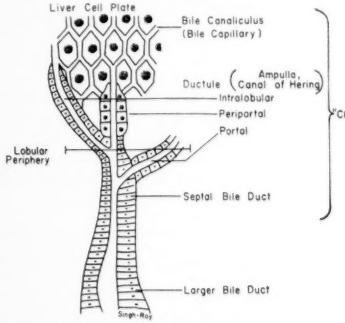

Fig. 1.—Illustration of nomenclature of intrahepatic biliary passages.

hepatic biliary ducts. Although the process is actually intrahepatic, its clinical and functional manifestations are those of an extrahepatic lesion.

Obstruction of Larger Intrahepatic Bile Ducts.—Compromise of the lumen of one main branch of the common hepatic duct without involvement of the other, for instance, by carcinoma, by stone, or after operation, produces elevation of the serum alkaline phosphatase level but no, or only transient, jaundice because the unobstructed part of the biliary system excretes the retained bile in a compensatory fashion. Rarely is obstruction of intrahepatic bile ducts outside of the smallest portal tracts widespread enough to produce persisting jaundice. Diffuse carcinomatosis of the liver and considerable parenchymal damage complicating local obstruction are exceptions. In very rare instances, xanthomatous areas around the intrahepatic bile ducts also produce cholestasis (fibroxanthomatous cirrhosis).[6] However, space-occupying lesions may produce focal bile stasis. Thus, morphologic evidence of bile stasis in liver biopsy specimens in the absence of jaundice suggests such a lesion, particularly metastatic carcinoma.

Obstruction of Septal Bile Ducts Within the Small Portal Tracts.—In a variety of conditions, the bile flow in septal bile ducts and ductules in the portal tract may be interfered with by compression, disruption of their continuity, or alteration. The evidence that accumulation of inflammatory exudate compresses the ductules is not convincing, since large amounts of exudate may accumulate without jaundice. Leukemic infiltration of portal tracts, even if severe, is not accompanied by jaundice. Similarly, severe portal fibrosis with portal hypertension, as in schistosomiasis, or granulomas, such as in sarcoidosis, does not necessarily produce jaundice. The only reliable morphologic evidence of a biliary obstruction within the portal tract is the absence of septal bile ducts or ductules within the inflamed or scarred portal tract. This occurs on a developmental basis in the rare instances of intrahepatic ductal atresia called acholangic biliary cirrhosis.[6] Of greater importance is the disappearance of ductules and ducts which has been considered the anatomic basis of the protracted jaundice occurring mainly in older women and frequently associated with hypercholesteremia and xanthomatosis. This lesion, as the most important representative of the syndrome of primary biliary cirrhosis (see below), has been designated as pericholangiolitic biliary cirrhosis [6] (fig. 3A). If the ductules are present, their morphologic alterations, namely, excessive proliferation, distortion, and fibrosis around them, are not as clearly established as causes of mechanical intrahepatic obstruction because similar features can apparently be found without jaundice. Such entities as obliterating cholangitis [7] and subacute cholangiolitic biliary cirrhosis [8] belong to this group. The French author Albot [9] lists two other entities: (1) obstructive cholangiolitis in the course of Rössle's nonobliterating diffuse cholangitis and (2) diffuse mesenchymatous hepatitis with nodular lymphomatosis of Hanot and Kiener. Further anatomic studies should identify the morphologic appearance of ductular alterations which exert an obstructing effect. Disruption of the ductules seems also to account for relatively acute jaundice in Hodgkin's disease.

Periportal Ductular Destruction.—In prolonged cholestasis of both intrahepatic and extrahepatic types, bile imbibition of the hepatic cells on the lobular periphery is associated with degenerative changes of these cells reflected also in the presence of granules giving a periodic acid Schiff reaction even after diastase treatment. This is accompanied by some inflammatory exudation and the appearance of collagenous fibers around these cells and their neighboring ductules, all of which disintegrate. The fibers seem to aggregate, forming a continuous collagenous barrier between these liver cell plates and their draining ductules (fig. 3*B*). Therefore, in

both intrahepatic and extrahepatic protracted cholestasis from any cause, a secondary intrahepatic mechanical obstructive component is added. It may account for persisting jaundice after surgical correction of a protracted extrahepatic obstruction.

The end stage of all the lesions listed is biliary cirrhosis, designated as primary biliary cirrhosis [10] if the extrahepatic biliary tract is not involved. The connective tissue may aggregate in the portal spaces or abound within the parenchyma (hypertrophic cirrhosis of Hanot). In the earlier stages, the altered reconstruction of the lobular parenchyma reflected in regenerative nodules and formation of septums connecting portal tracts and central canals is still in the background, and the manifestations of cholestasis dominate the picture. In advanced stages, all signs and symptoms of cirrhosis are present.

Intrahepatic Cholestatic Component of Hepatic Disease.—In almost all hepatic diseases associated with diffuse liver cell injury, the degree of jaundice may not be directly related to the degree of hepatocellular damage or that of hemolysis. In such instances it is well correlated with the degree of cholestasis as morphologically seen in the liver and with the results of hepatic tests assumed to reflect cholestasis. These are increases of serum alkaline phosphatase activity and total serum cholesterol and reduction of fecal and urinary urobilinogen. On this evidence rests the assumption that an intrahepatic cholestatic component accounts at least for part of the jaundice in various types of hepatitis and cirrhosis.[11] Between the two extremes of liver cell injury without cholestasis and cholestasis without liver cell injury, all degrees of combinations may occur in different patients and in different stages of the same disease in an individual patient.

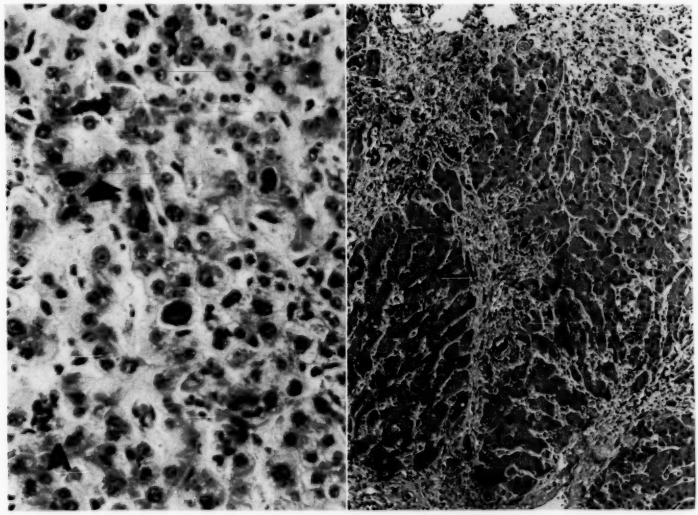

Fig. 2.—*A*, bile stasis in center of lobule reflected by presence of bile in form of various sized granules in liver cells (*arrow*), in casts in bile canaliculi, and in Kupffer cells. Hematoxylin and eosin stain (× 240). *B*, intrahepatic bile stasis in postnecrotic cirrhosis evidenced by microcalculi in proliferated ductules and in septal bile duct (*arrow*). Hemotoxylin and eosin stain (× 63).

Intrahepatic Cholestasis Without Structurally Demonstrable Causes

Conditions falling under the heading of intrahepatic cholestasis without structurally demonstrable causes are of particular differential diagnostic importance, and far more frequent clinical examples are seen than in the group with obvious obstruction. However, the lack of an established pathogenesis permits only an enumeration of examples rather than a rational classification.

The question of surgery because of assumed extrahepatic biliary obstruction may arise, but here liver biopsy is helpful in clarifying the nature of the disease process. In rare cases of viral hepatitis with an otherwise typical morphologic picture, cholestasis is clinically in the foreground.[12] More frequently, cholestasis predominates in one phase of an otherwise clinically typical instance of viral hepatitis.[4] Cholestatic features may also complicate large fatty livers with jaundice, diffuse septal cirrhosis,

and particularly active stages of postnecrotic cirrhosis in which the deposition of microcalculi in ductules may be conspicuous. A cholestatic component may also be in the foreground of various hepatic disorders of vague etiology, such as "toxic hepatitis" occurring after operation or in the neonatal period.

Intrahepatic Cholestasis as Dominant Feature of Hepatic Disease.—Probably the most difficult differential diagnostic problems are presented by a group of cases in which cholestasis without a tangible anatomic substrate is clinically, functionally, and structurally in the foreground. Liver cell damage, if present, is relatively mild or is frequently the result of the cholestasis if feathery degeneration of liver cells is seen. In the early stages, inflammatory reactions in the parenchyma and in the portal tracts may be absent. They are regularly present after several weeks' duration and the term cholangiolitis then appears appropriate.[11] They probably are the result of the lesion rather than its cause.

In chronic stages the picture of pericholangiolitic biliary cirrhosis previously referred to may appear. However, the incidence of the progression of the cases of this group into primary biliary cirrhosis still remains to be established. In view of the absence of characteristic inflammatory changes, liver biopsy may not be of great assistance in the separation from extrahepatic biliary obstruction. It may become more helpful but also more dangerous after several weeks. Then extrahepatic biliary obstruction may have produced diffuse dilatation of the entire biliary tree. This mechanical pressure effect of hydrohepatosis is histologically reflected in the pathognomonic findings of bile infarcts and bile extravasation. Drugs of quite divergent nature chemically are reported, in increasing numbers, to produce cholestasis. In another group of cases, at present better designated as idiopathic, the etiology is unknown or at best doubtful.

Drug-Induced Intrahepatic Cholestasis: Of the various drugs producing intrahepatic cholestasis associated with little or no liver cell injury, chlorpromazine (Thorazine) seems to be the most important in recent years from the point of view of incidence.[13] In cases of intrahepatic cholestasis produced by arsphenamine,[1] chlorpromazine, para-aminosalicylic acid,[14] thiouracil, and sulfanilamide, portal infiltration has been present. In cases produced by methyltestosterone,[15] norethandrolone (Nilevar),[16] para-aminobenzoyl caffein hydrochloride, methimazole (Tapazole), and sulfadiazine, portal infiltration has not been present. Although all of the drugs produce the same structural and functional manifestations of cholestasis, only some elicit at least temporary inflammatory reactions in the portal tracts reflected in accumulation of lymphocytes, histiocytes, and segmented leukocytes,

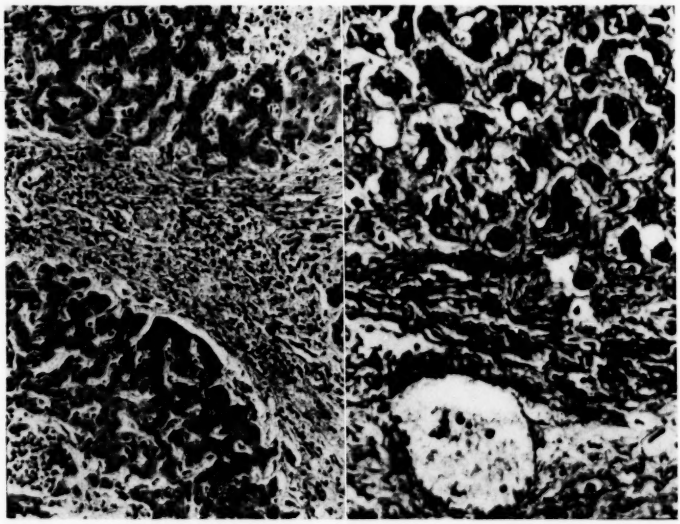

Fig. 3.—A, absence of bile ducts and ductules in trabeculae of pericholangiolitic biliary cirrhosis with xanthomatosis. Hematoxylin and eosin stain (× 120). *B*, aggregation of collagenous fibers on border between portal tract and parenchyma containing degenerating liver cells in secondary biliary cirrhosis after stricture of common bile duct. Mallory aniline blue stain (× 240).

many of which are eosinophilic, associated with proliferation of ductules and circulating eosinophilia (fig. 4A). This lesion has been called allergic cholangiolitis [4] and has been implicated in the development of the cholestasis.

However, this portal reaction is absent, for instance, in jaundice produced by methyltestosterone [15] or norethandrolone [16] (fig. 4B). It may be present without jaundice in reactions produced by chlorpromazine or para-aminosalicylic acid.[14] Moreover, morphologically identical reactions may occur without previous drug therapy in random liver biopsy specimens [16] or in systemic hyperergic reactions without jaundice. In patients dying with progressive cholestasis from chlorpromazine treatment, the portal tract may be entirely normal even if preceding liver biopsies demonstrated portal reactions.[11] It thus appears that cholestasis and portal inflammatory reactions (hyperergic or not) are independent phenomena. In a very few patients exposed to chlorpromazine [17] or arsenicals,[18] transition into what has been called primary biliary cirrhosis with xanthomatosis has been reported.

Idiopathic Intrahepatic Cholestasis: The ill-defined group of patients with idiopathic intrahepatic cholestasis includes those with possible endocrine disturbances, particularly if jaundice develops during the menarche or menopause, and patients with suspected viral hepatitis,[2] at least on epidemiologic grounds, in which case it is an extreme of the condition discussed in the section on cholestatic component of hepatic disease.

Pathogenesis

Intrahepatic biliary obstruction as a mechanism producing cholestasis requires no further consideration. Since intrahepatic biliary obstruction develops in chronic stages of all forms of cholestasis, the pathogenesis of acute cholestasis in both the pure form and as a component of hepatic disease is the major problem. Much has been written about this since Naunyn assumed an alteration of the polarity of the bile flow from liver cells into the blood stream. Recent morphologic and biochemical investigations have pointed to the probable site of cholestasis although not to its mechanism. The morphologic integrity of the liver cells and the usually normal results of hepatic tests indicating hepatocellular damage as well as the presence of bile within the intraparenchymal biliary passages speak against impairment of hepatic cell function. The bilirubin in the serum gives a direct van den Bergh reaction and, therefore, interference with its glucuronide conjugation is unlikely.

Since no evidence exists for any anatomic alteration of the septal or larger bile ducts, cholestasis had been localized in the bile canaliculi or ductules (fig. 5). The possibility that an actual obstruction

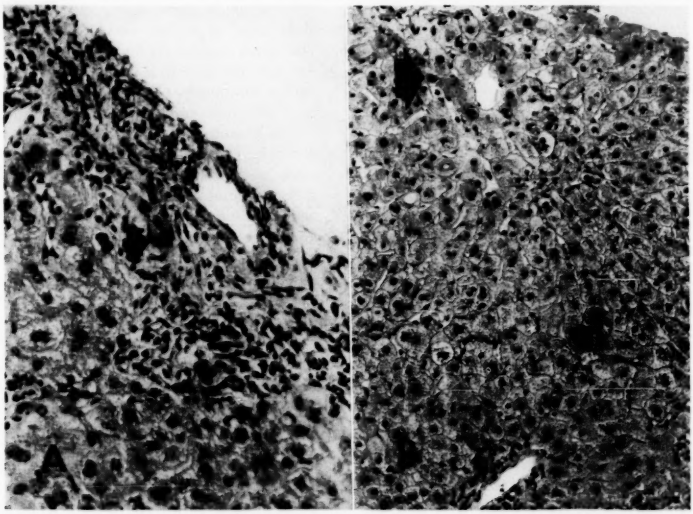

Fig. 4.—*A*, accumulation of segmented leukocytes, including many eosinophils, histiocytes, and lymphocytes and proliferation of ductules (*arrow*) in edematous small portal tract indistinctly delineated from surrounding parenchyma in liver biopsy specimen from patient with jaundice occurring after administration of chlorpromazine. Hematoxylin and eosin stain (× 240). *B*, intrahepatic cholestasis in centrolobular zone (*arrow*) in absence of alterations of portal tract in biopsy specimen from patient who had received norethandrolone. Hematoxylin and eosin stain (× 120).

exists within the bile canaliculi or ductules by either swollen, disorganized, or regenerating liver cells, or by bile plugs in the canaliculi or ductules, is negated by the presence of bile, at least in some cases, along the entire length of the bile canaliculi and ductules. Occasionally bile may even be seen under these circumstances in the form of microcalculi in the septal bile ducts. These findings suggest that the bile is inspissated or altered in its constitution. This is supported by the frequent occurrence of biliary concrements in the extrahepatic biliary ducts which gave rise to the term "inspissated bile syndrome" in children. They are more probably a reflection of altered bile rather than the cause of obstruction, especially since the biliary passages are not dilated.

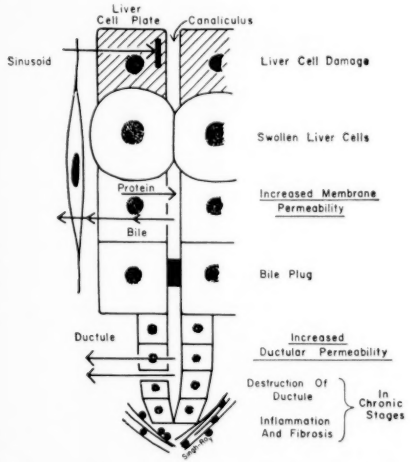

Fig. 5.—Illustration of possible mechanisms responsible for intrahepatic cholestasis.

Inflammation around the ductules and ducts in the portal tract (cholangiolitis) has already been excluded as a pathogenetic factor since it is not always present in cholestasis and may be present in the absence of jaundice. Thus, a permeability change, as previously assumed,[2] appears to account for intrahepatic cholestasis. Permeability may be increased in two opposite directions. Regurgitation of biliary substances from canaliculi or ductules may account for jaundice and possibly also for periductular inflammatory reactions. Moreover, a relatively greater backflow of fluid rather than solids may explain the dehydration and inspissation of bile with formation of bile plugs. Increased permeability in the other direction with oozing of protein from the liver cells into the bile (albuminocholia)[3] may increase the viscosity of the bile, leading to its inspissation. Material, apparently carbohydrate-protein complexes, is stained with the periodic acid Schiff reaction around bile plugs.

The alteration of the bile by possibly both dehydration and albuminocholia may best explain acute intrahepatic cholestasis. Differences in the conjugation of bilirubin in the bile deserve further study. The permeability alteration seems to be localized in the hepatic cell membrane lining the bile canaliculus and possibly also in the ductules. Further study of the microvilli visible under the electron microscope in these locations may clarify the time-worn problem of the pathogenesis of hepatogenous jaundice.

Conclusions

Intrahepatic cholestasis results from mechanical obstruction or has no demonstrable pathogenesis. The latter process seems to be a characteristic reaction of the liver to a variety of injuries. It may be only a component of a hepatic disease with structural and functional involvement of the liver cells and is, therefore, found in any type of cirrhosis or hepatitis. On the other hand, intrahepatic cholestasis may be an independent phenomenon which either is induced by drugs or is of unknown (idiopathic) etiology. The acute and subacute stages of nonobstructive intrahepatic cholestasis, more so than with demonstrable mechanical obstacles, present a difficult differential diagnostic problem because of similarity to the "surgical" type of jaundice in extrahepatic biliary obstruction. Clinical observations and hepatic tests may not provide the answer, while liver biopsy is helpful only in the presence of positive findings such as the "hypergergic" type of portal inflammation in drug-induced cholestasis or the effects of hydrohepatosis in mechanical obstruction. Surgical exploration or percutaneous cholangiography may still be a diagnostic last resort.

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CLINICAL ASPECTS OF JAUNDICE RESULTING FROM INTRAHEPATIC OBSTRUCTION

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Currently drug sensitivity reactions are responsible for most instances of self-limited jaundice due to primary intrahepatic cholestasis. Icterus associated with chlorpromazine therapy represents a classic example. The development of jaundice after the drug therapy is discontinued and the occurrence of prolonged jaundice are illustrated in two patients as uncommon but noteworthy examples of this drug idiosyncrasy. In a third case, a 54-year-old man became jaundiced after four months' medication with methyl testosterone. A chronic progressive form of jaundice resulting from intrahepatic obstruction is exemplified by a 47-year-old woman with primary biliary cirrhosis of unknown etiology. The slowly increasing rise of the serum bilirubin level was temporarily reversed by steroid therapy. This effect was more likely due to the suppression of a mild concomitant hemolytic than to an effect on her liver disease. Subsequently the serum bilirubin level rose again. Death occurred after hemorrhage from esophageal varices.

The various disorders associated with jaundice resulting from intrahepatic obstruction represent a major clinical problem in adult patients with icterus. Fundamentally all instances of jaundice not caused by a gross mechanical obstruction to the free outflow of bile from the liver represent intrahepatic obstruction. Popper's classification of jaundice,[1] i. e., according to impairment or non-impairment of bile flow, is a helpful approach in discussing the mechanisms involved. In clinical practice, instances of jaundice without impairment of bile flow (jaundice associated with over-production of free bilirubin as in hemolytic disorders and retention jaundice, as in constitutional hepatic dysfunction), can usually be recognized without undue difficulty. Chronic idiopathic jaundice (Dubin-Johnson syndrome) is probably not associated with a significant quantitative reduction in total bile flow despite the mild degree of regurgitation jaundice that characterizes the condition. The diagnosis can be established by clinical study and liver biopsy. It is not customarily included in discussions of jaundice resulting from intrahepatic obstruction.

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Patients with impaired bile flow exhibit regurgitation jaundice; increased amounts of both conjugated and free bilirubin are present in the blood serum. The major problems in differential diagnosis are encountered in patients with regurgitation jaundice. The term cholestasis is useful in a descriptive sense for a discussion of the phenomenon of impaired bile flow in the liver itself. Cholestasis produced by extrahepatic obstruction, i. e., "surgical jaundice" due to gallstones, cancer, or stricture, usually presents a fairly well-defined clinical, biochemical, and morphologic picture. On the basis of careful clinical studies, the existence of extrahepatic biliary obstruction can be correctly predicted preoperatively in 90% of surgical cases. The problem cases encountered in the 10% group are mainly in patients who have moderately severe hepatocellular damage associated with the obstruction or who have unusual types of obstructing lesions.

Cholestasis resulting from an intrahepatic obstruction to the flow of bile presents a more formidable problem in diagnosis. Intrahepatic cholestasis is a component in the majority of patients who exhibit hepatocellular degeneration, i. e., viral hepatitis, toxic liver injury, and the various forms of cirrhosis.[1] When the component of hepatocellular degeneration predominates, a correct diagnosis of the hepatic condition can usually be established without undue difficulty. The clinical features are fairly distinctive, and the biochemical and the morphologic changes (as seen in a biopsy specimen) are revealing. Unfortunately the component "cholestasis" is not accompanied by a specific recognizable morphologic lesion; the deposition of bile pigment in the liver cells and in the canaliculi is nonspecific. Intrahepatic cholestasis may at times be the major or predominant component of a liver disorder that ordinarily is considered to be a typical example of jaundice due to hepatocellular degeneration.

Thus the physician is occasionally confronted by a patient with viral hepatitis or cirrhosis in whom the degree and duration of icterus and other evidences of biliary obstruction seem out of proportion and unusually prominent when compared with the average or classic case. This is reflected in the clinical picture; i. e., the patient may be more jaundiced than ill. It is reflected in the biochemical picture; i. e., the bilirubin, alkaline phosphatase, and lipid pattern indicate obstruction while the quantitative and qualitative changes in the serum proteins characteristic of hepatocellular damage are often minimal. Yet, even when cholestasis is a major component in cirrhosis or in viral hepatitis, an experienced pathologist can usually recognize the basic underlying disturbance by a careful study of the liver biopsy.

Gall and Braunstein[2] emphasized that in viral hepatitis the fundamental morphologic features can be recognized in biopsy specimens, even though the pathologist may not be able to predict which patients exhibit clinical or biochemical manifestations simulating excretory impairment and which patients exhibit the accepted clinical and biochemical evidences of hepatocellular degeneration. The recognition of intrahepatic cholestasis as the predominant component of certain liver disorders associated with jaundice can often be accomplished by analyzing a combination of clinical, laboratory, and histological evidences. It must be admitted that some patients do present extremely complex problems. The variables inherent in extrahepatic biliary obstruction (cholestasis with hepatocellular damage as a variable component) and the hepatitis-cirrhosis-toxic liver injury group (hepatocellular degeneration with cholestasis as a variable component) are very great indeed. At times the correct diagnosis cannot be established until the exact status of the extrahepatic bile duct system is determined.

In certain patients cholangiography must be performed. In these complex situations the safest course is to treat the patient as a medical problem for four to six weeks before resorting to operation. The arbitrary period of study and medical treatment of these diagnostic problem cases admittedly constitutes a hardship for the patient who ultimately proves to have a surgical lesion. However, it is likely to be lifesaving for the patient with medical jaundice in whom early surgical intervention is not only unrewarding but actually hazardous.

Jaundice due to intrahepatic obstruction is not limited to patients with hepatocellular degeneration, i. e., cirrhosis, viral hepatitis, or toxic liver injury. Manifestations of cholestasis may be the sole component discernible in certain liver disorders in which the liver cells appear normal and the extrahepatic duct system is completely patent, i. e., primary intrahepatic cholestasis. The patient with jaundice due to chlorpromazine sensitivity is a classic example. A number of drugs have been incriminated in the hypersensitivity reactions that produce primary intrahepatic cholestasis. In rare instances no cause can be definitely established.

The basic mechanism involved in primary intrahepatic cholestasis is unknown. If a single mechanism is involved, it is presumed to be a regurgitation of bile back through morphologically intact "cholangioles." (The term cholangiole has been used broadly to include the biliary canaliculi, the ductules, and the terminal ducts.[3] As used in current American literature the term presumably includes the ductules—intralobular and perilobular ducts—and the interlobular ducts, but not the

canaliculi.) One must assume that a functional derangement in the cholangioles permits biliary substances to leak back into the tissues and eventually to regurgitate into the lymph and blood. This explanation is invoked to account for the presence of bile thrombi in the canaliculi up to but not beyond the ductules, the apparently normal histological appearance of the ductules and ducts and the pericholangiolitis. The inflammatory reaction is presumably due to irritation produced by substances in bile.

The explanation has been offered that an increased permeability of the cholangioles favors an increased absorption of water with a resultant inspissation of bile. The occurrence of bile plugs or thrombi, so prominent in intrahepatic cholestasis, is thought to be on this basis. Bile thrombi themselves are not believed to be the fundamental cause of the intrahepatic obstruction. One must accept the fact that the morphologic evidences of cholestasis, i. e., the bile staining, the bile plugs, the inflammatory reaction, and the evidences of parenchymal cell injury (usually very minimal and insignificant in primary intrahepatic cholestasis) are probably secondary to the stasis of bile rather than its cause.

The critical student of the subject may not be entirely satisfied with the explanation that a functional impairment of the cholangioles, i. e., an increased permeability, is responsible for jaundice due to intrahepatic obstruction. This has been regarded as a plausible explanation to account for the available biochemical and histological observations. The inability to produce a liver lesion in an experimental animal that completely mimics primary intrahepatic cholestasis as seen in man is a distinct handicap in fundamental investigations of this important subject. The experimental studies of Hanzon [4] dealing with basic mechanisms involved in regurgitation jaundice did not indicate that the ductules or ducts exhibited an undue vulnerability as a site of bile escape. In graded liver cell injury and in the early stages of extrahepatic obstruction, regurgitation of bile (visualized by virtue of fluorescent uranin) was observed to occur directly from intact canaliculi and from morphologically intact liver cells.

The apparent absence of a specific morphologic lesion in primary intrahepatic cholestasis disturbs the pathologist in his attempts to explain the pathogenesis of the disorder. The absence of a specific lesion also constitutes a very real obstacle in the practical problem of establishing the diagnosis on the basis of a liver biopsy specimen. The similarity of the histological appearance of the liver irrespective of whether cholestasis is due to intrahepatic or extrahepatic obstruction has been emphasized repeatedly. At times the hydromechanical effects of extrahepatic obstruction are sufficient to produce specific morphologic changes that have diagnostic value. However, when liver biopsies are performed early, i. e., within the first two or three weeks of the onset of jaundice, the pathologist may not be able to make the distinction.

Primary intrahepatic cholestasis presents a clinical picture that may be easily confused with some forms of extrahepatic biliary obstruction, since the features are often those of icterus and pruritus without signs of toxicity or sepsis. The liver tests are not usually distinctive; the alkaline phosphatase and lipid levels are elevated in both conditions, and the abnormalities in the proteins (quantitative or qualitative) are usually minimal in each type. Fortunately, many instances of intrahepatic obstruction, especially cases of drug-induced jaundice, are self-limited and soon relent. A correct diagnosis can often be established during the course of clinical observation and medical treatment. Occasionally cases of protracted jaundice due to primary intrahepatic cholestasis are encountered, and an operative cholangiogram may be required to establish the diagnosis with absolute certainty. In selected instances this may be performed under local anesthesia through a small abdominal incision.

Acute (Self-Limited) Forms of Jaundice Resulting from Intrahepatic Obstruction

Drug reactions are responsible for the majority of instances of primary intrahepatic cholestasis that are currently encountered in clinical practice. The characteristic histopathological and biochemical features of this type of reaction were described in 1940 by Hanger and Gutman in cases of arsphenamine sensitivity, and in the ensuing 18 years [5] a number of other drugs have been incriminated as causative agents. Jaundice due to chlorpromazine has been the most common cause of this reaction in recent years.

Jaundice due to Chlorpromazine.—The incidence of jaundice due to chlorpromazine (Thorazine) hydrochloride is stated by the manufacturer to be "low," but in view of its administration to more than 10 million patients, even a low incidence of this reaction results in a large number of individuals with icterus. There have been many opportunities to study the problem; the literature has been reviewed in recent reports.[6] Although the pattern of reaction has varied somewhat, the majority of patients develop jaundice during the second or third week of the drug administration. The onset of jaundice is often preceded by three or four days of prodromal symptoms that include fever, malaise, anorexia, and indefinite gastrointestinal symptoms. At times patients experience mild degrees of abdominal pain at the onset. The jaundice is typically obstructive in type with dark urine and light stools.

With the onset of jaundice many of the symptoms disappear, and, save for pruritus, the patients become relatively comfortable. The prostration that usually attends viral hepatitis is customarily lacking in patients with jaundice due to chlorpromazine. Fortunately, the intrahepatic obstruction to bile flow usually relents within a few weeks to two months, and the patients recover uneventfully. Although most observers regard the disorder as a hypersensitivity phenomenon, there are many aspects of the problem that remain obscure. In a few patients the drug can be administered again without producing a recurrence of icterus, and yet in other patients an exquisite hypersensitivity to the agent has been demonstrated.

The histopathology of jaundice due to chlorpromazine is characteristic and represents the typical picture of primary intrahepatic cholestasis. The findings usually observed are centrolobular bile staining, bile casts or plugs predominately centrolobular in location, and minimal evidence of periportal or periductular inflammation. When present, the latter is usually nonseptic in character. The occasional occurrence of some eosinophils scattered among the round cells in the infiltrate lends weight to the concept that the reaction may be allergic in nature.

The laboratory tests in jaundice due to chlorpromazine follow a fairly uniform pattern in the majority of cases. The regurgitation jaundice that occurs is characterized by elevations of both direct and indirect reacting types of serum bilirubin. The degree and duration of the hyperbilirubinemia varies greatly. An increase in the level of the alkaline phosphatase is an almost constant phenomenon; this often precedes the elevation of the serum bilirubin level.[7] The cephalin cholesterol flocculation test, the thymol turbidity reaction, and similar liver tests are usually normal in chlorpromazine-induced jaundice.

Several unusual aspects of the chlorpromazine-induced jaundice problem warrant comment. The occurrence of jaundice some days after the drug therapy has been stopped deserves emphasis. Cases have been described in which jaundice developed 14 to 19 days after chlorpromazine therapy had been discontinued, even though the patient had received the drug for only 5 or 6 days.[8] The diagnosis of intrahepatic cholestasis was confirmed by a liver biopsy secured at the time of operation. In each instance the common bile duct was patent. The apparent late development of jaundice after chlorpromazine therapy has been discontinued has also been witnessed in a patient on the medical service of the University of Minnesota Hospitals. In this instance jaundice was first noted approximately three weeks after the drug was withdrawn. The icterus reached its peak in another three weeks and gradually relented. Icterus lasted approximately two months. The patient was admitted late in the course of the illness, and a liver biopsy was not deemed necessary.

A review of the available liver tests that had been performed indicated the rather characteristic pattern exhibited by patients with chlorpromazine-induced jaundice. Throughout the period of icterus, the bilirubin, phosphatase, and the serum lipid levels were elevated and the cephalin-cholesterol flocculation and thymol turbidity test remained normal. Although the diagnosis was not established with absolute certainty, the clinical course strongly suggested a delayed drug reaction as the cause of jaundice. Such episodes are admittedly uncommon, but they do emphasize the need for a careful inquiry regarding use of recent drugs in all jaundiced patients.

In a few reported instances, jaundice due to chlorpromazine has been very protracted. A remarkable example was reported by Myers and associates.[9] A man, aged 31, developed jaundice and pruritus after receiving the drug for two weeks. He remained jaundiced for 20 months. Five months after the onset of icterus, the patient developed many of the characteristic features of primary biliary cirrhosis, including extensive xanthomata and splenomegaly. Eventually the marked hypercholesterolemia declined and the xanthomata disappeared. Though the patient's jaundice entirely cleared, the spleen remained enlarged and fear was expressed that his cirrhosis might yet progress. Instances of prolonged jaundice due to chlorpromazine have been observed by others. In one reported series,[10] a patient remained jaundiced for 13 months, and a second patient who became jaundiced during early pregnancy remained icteric for eight and one-half months.

I have had an opportunity to see in consultation one patient in whom jaundice lasted for an entire year. The patient received chlorpromazine in the treatment of severe vomiting during the first trimester of her pregnancy. Jaundice developed 17 days after the drug therapy was first started. The patient's jaundice persisted throughout her pregnancy. After an uneventful delivery in December, 1956, the icterus increased in intensity and was followed by a rise in the blood cholesterol level. Fortunately a gradual remission occurred, and by July, 1957, the jaundice had virtually disappeared. Whether or not protracted jaundice is more prone to develop when this form of drug sensitivity occurs during pregnancy is not known. It would seem a wise precaution to discontinue use of the agent very promptly in any pregnant woman receiving chlorpromazine when even a slight rise in the serum phosphatase or bilirubin level indicates the possible onset of this drug reaction.

Jaundice due to Methyl Testosterone.—The clinical and histological observations in patients who have developed jaundice during the course of methyl testosterone therapy have been described by several observers.[11] The following case, studied with other physicians in 1951, illustrates the occurrence of intrahepatic biliary obstruction in a patient who received methyl testosterone orally for a period of four months.

CASE 1.—A 54-year-old white man was admitted to the medical service of Drs. Altnow and Bowers at the Eitel Hospital in Minneapolis, March 27, 1951. The patient was referred for study and treatment of jaundice that had been present for one month. The patient had experienced mild indigestion and fatty food intolerance for the preceding two months. Physical examination revealed a deeply jaundiced man; the liver was palpable just below the costal margin. There were no stigmata of cirrhosis present. Routine laboratory studies yielded normal results. The icteric index was 130 units; the prothrombin time was 41% of normal. After a single injection of vitamin K the prothrombin time returned to normal. The stools appeared acholic.

On March 29, a surgical exploration was carried out by Dr. W. I. Nelson. The liver was found to be smooth but deeply bile stained. The gallbladder and bile ducts were collapsed but patent. A T-tube was inserted into the common duct, and a cholangiogram was secured. This revealed that the larger intrahepatic ducts were patent and a free flow of contrast media through the common bile duct into the duodenum was demonstrated. A biopsy of the liver was secured at the operation. Postoperatively small amounts of bile appeared in the T-tube after several days. The patient's jaundice persisted for some time. The T-tube was removed after two weeks.

The liver biopsy revealed bile staining most marked in the center of the lobules. A minimal degree of liver cell damage was apparent in the centrolobular portion where slight disorganization of the cell plates was evident. In general, the architecture of the liver was well preserved. Although numerous bile thrombi were seen, no "bile lakes" were noted. The larger bile ducts were empty. Inflammatory exudate was inconspicuous. The pathologist, Dr. Craig Freeman, termed the lesion an intrahepatic obstruction of unknown etiology. Further inquiries regarding antecedent drug therapy were made. It was learned from the referring physician that the man had received methyl testosterone, 15 mg. per day, from October, 1950, to February, 1951. The medication was discontinued with the onset of jaundice.

Two weeks after operation a series of liver tests was repeated. These were secured during the eighth week of the patient's jaundice, and the results were as follows: serum bilirubin level (one minute) 5.4 and (total) 8.5 mg. per milliliter; cephalin-cholesterol flocculation, negative; thymol turbidity, 1 unit; zinc turbidity, 8 units; serum alkaline phosphatase level, 27.6 King-Armstrong units; serum cholesterol level, total, 298 mg. per 100 ml.; and feces urobilinogen level, 51 mg. per day. The patient's jaundice slowly receded; on May 20, 1951, the total serum bilirubin level was 2.7 and the total cholesterol level, 288 mg. per milliliter. The patient made an uneventful recovery, and the jaundice disappeared by July, 1951. The patient has remained well subsequently.

It seemed evident that this patient developed painless jaundice as a result of intrahepatic cholestasis brought about by a drug hypersisitivity reaction. In most of the reported instances of jaundice associated with methyl testosterone, icterus has appeared after two or three months of therapy. This unusual and admittedly uncommon reaction seems to be limited to patients receiving methyl testosterone; as far as is known it has not been reported in patients receiving testosterone propionate.

Methyl testosterone may be given to relieve itching in patients who have obstructive jaundice.[12] In my experience this usually causes a further rise in the serum bilirubin level. The mechanism by which this agent acts on the liver is unknown. In selected patients with jaundice, methyl testosterone may be administered in an attempt to relieve pruritus, provided such patients are willing to accept the risk of increasing icterus and probable aggravation of any existing tendency toward edema formation. To some patients with intolerable itching this price they must pay for relief of their distress does not seem too high. The following case illustrates the aggravation of the jaundice concomitant with the relief of the pruritus in a patient with secondary (cholangitic) biliary cirrhosis.

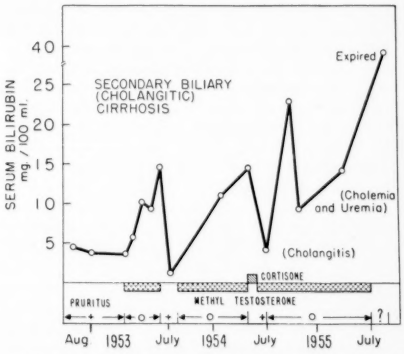

Fig. 1 (case 2).—Jaundice and severe pruritus in patient with biliary cirrhosis. Oral methyl testosterone therapy relieved itching but was accompanied by increase in degree of icterus.

CASE 2.—A 69-year-old woman suffered an injury to the common bile duct at the time of a cholecystectomy performed by her private physician in 1950. After a stormy postoperative course the patient developed marked jaundice. Five months later an experienced surgeon operated on the patient and succeeded in anastomosing the right and left hepatic ducts directly to the duodenum. Eighteen months later the patient had an episode of ascending cholangitis. She was first treated at the University of Minnesota Hospitals in August, 1952. After intensive antibiotic therapy and drainage of a right subphrenic space abscess, the patient recovered; low-grade jaundice and intense pruritus persisted. In February, 1953, the patient was given methyl testosterone in amounts sufficient to control her pruritus. This usually amounted to 20 mg. per day.

As shown in figure 1, the patient did obtain relief of her pruritus, but the serum bilirubin level rose. When the drug therapy was discontinued, the jaundice receded and the pruritus returned. These observations were repeated again in 1954. The drug therapy was discontinued in May, 1954, and the patient received cortisone for one month. Although the serum bilirubin level fell, the rate of decline was no faster than previously noted without cortisone. The development of gastrointestinal distress and bleeding necessitated the discontinuing of cortisone therapy. The patient's final year of life was marked by recurrent attacks of cholangitis; this made it difficult to determine how much of the elevation of the serum bilirubin was due to the administration of methyl testosterone and how much to an aggravation of her underlying disease. She eventually developed cholemia and uremia and died.

The case illustrates the aggravation of a preexisting jaundice when methyl testosterone was given to obtain relief of distressing pruritus.

In addition to the agents mentioned, other drugs have been held responsible for the occurrence of jaundice resulting from intrahepatic obstruction. The incidence of such reactions has been far less than with chlorpromazine. The experiences emphasize the need for a careful evaluation of drugs recently administered when one first examines a jaundiced patient. Jaundice due to intrahepatic obstruction resulting from a drug sensitivity reaction may so closely mimic obstructive jaundice produced by gallstone or tumor that the examiner may easily be misled.

An occasional patient with viral hepatitis may exhibit features of prolonged regurgitation jaundice and thus simulate bile duct obstruction. The value of needle biopsy of the liver in establishing the existence of viral hepatitis as the underlying or fundamental disorder in such patients has been recently emphasized.[13] The histopathological changes may not be correctly interpreted unless the specimen is examined by an experienced pathologist who has taken a particular interest in this type of differential diagnosis.

Chronic (Progressive) Forms of Jaundice Resulting from Intrahepatic Obstruction

A classic example of a chronic form of intrahepatic obstructive jaundice is represented in the patient with primary biliary cirrhosis.[14] The victims of this disorder are usually well-developed, well-nourished, middle-aged women who exhibit melanotic pigmentation of the skin. On examination the sclerae are often found to be icteric and the liver enlarged, readily palpable, but seldom tender. The spleen is also enlarged. The skin over the arms and legs, thickened and revealing evidences of self-inflicted scratch marks, attests to the presence of prolonged pruritus. Such patients may or may not exhibit xanthelasma and xanthoma.

The case histories of 30 adult female patients studied at the University of Minnesota Hospitals during the 12-year period 1945 to 1956 have been recently reviewed. In each instance most of the typical features of primary biliary cirrhosis existed. Because of the relative rarity and long duration it is difficult to witness the entire natural course of this chronic disorder in more than a few instances. In the cases reviewed there was no conclusive evidence that a single entity was represented, despite the similar clinical findings exhibited by most of the patients. Nearly all students of the disease have observed its striking predilection for adult women.

The disease often begins so insidiously that it is difficult to determine the onset. This was estimated to be before age 40 in eight instances in the series reviewed; 15 patients appeared to develop the disease between the ages of 40 and 60 years. Three were beyond the age of 60 years when the first symptoms appeared. The exact time of onset could not be determined in four cases. No clear-cut relationship to menses, to pregnancy, or to the menopause was evident. The estimated duration of the disease was from 3 to 16 years in the patients who could be followed.

The existence of primary biliary cirrhosis can be suspected on the basis of the characteristic symptoms of fatigue and pruritus and the physical signs of pigmentation of the skin and enlargement of the liver. It should be emphasized that detectable jaundice may not develop until some time after the onset of the disease. A pathological diagnosis can usually be established during life if an adequate liver biopsy specimen can be obtained. The earliest lesion that can be recognized is a pericholangiolitis, initially associated with bile ductule proliferation. Later the number of bile ductules appears to decrease, and the pathological findings in the liver become increasingly complex as the disease advances.[14]

The etiology of the disease is unknown; MacKay's recent observations[15] offer promise of new insight into this obscure illness. In the majority of instances the disorder appears to be relentlessly progressive once it is established. The late stages are characterized by evidences of portal hypertension and hepatic insufficiency. At present, no specific remedies are known; treatment must be symptomatic and supportive. The clinical management of the patient with primary biliary cirrhosis poses a very difficult problem for the attending physician. In the early phase of the disease, a phase which incidentally may last 3 to 10 years, the problems of the control of itching and fatigue are prominent. In some patients the prolonged elevation of the blood cholesterol level leads to xanthoma formation, with its associated discomfort and disfigurement. As the disorder progresses and slow deterioration of liver function becomes manifest, the elevated blood lipid levels often diminish. The prolonged exclusion of bile from the intestine in

some instances may lead to skeletal demineralization. Severe bone pain was noted in three of the patients studied in the present series of 30 cases. Each patient obtained some relief from bone pain when the calcium and vitamin D intake was augmented.

The late phase of the clinical course of primary biliary cirrhosis is marked by the problems of liver insufficiency with edema and ascites formation. Portal hypertension and the occurrence of hemorrhage from esophageal varices is a prominent feature in some instances. The following case has been selected from the series reviewed to illustrate this point and also to emphasize another feature. In assessing the significance of the degree of jaundice in any given patient, it is necessary to consider the total daily pigment production and the excretory ability of the liver. In most of the common forms of cirrhosis, for example, a primarily fatty cirrhosis in an alcoholic patient or an idiopathic postnecrotic cirrhosis in a young woman, an increase in the depth of jaundice usually signifies increasing parenchymal cell damage and is an ominous sign.

In primary biliary cirrhosis, during the early phase at least, the depth of jaundice does not necessarily reflect the same degree of liver cell impairment but rather the inability of the intrahepatic biliary system to excrete the daily bilirubin load. Such patients are barely able to excrete the normal daily load of bilirubin produced by the normal daily rate of red blood cell destruction. If there is even a slight increase in the daily production of bilirubin, i. e., a mild hemolytic process related to the presence of congestive splenomegaly, the degree of jaundice may become quite intense. The depth of jaundice must be considered in relationship to the factors of bilirubin production and the impaired ability of the liver to excrete pigment.

Case 3.—In February, 1955, this 47-year-old woman was referred to the medical service of the University of Minnesota Hospitals because of chronic jaundice, pigmentation, and pruritus. The patient had first consulted a physician in August, 1954; jaundice was observed and bed rest advised on the presumptive diagnosis of hepatitis. There were no known contacts with cases of viral hepatitis in the community, and none had occurred in the family. Six weeks of bed rest failed to produce an alteration in the status of the patient. In October, 1954, she was more thoroughly investigated because the low-grade jaundice persisted. Cholecystography was performed; this revealed a normally functioning gallbladder. A needle biopsy of the liver was interpreted by the pathologist as showing "benign low grade hepatitis." The blood serology report at this time was "V.D.R.L. doubtful positive 1-16" and "Wassermann doubtful positive." The patient's condition remained unchanged despite various measures used.

The admission examination of the patient in February, 1955, revealed an icteric and pigmented woman in no apparent distress save for pruritus. The liver and the spleen were palpable. No ascites was noted. Skin lesions on the legs were considered to be those of lichen planus; this diagnosis was subsequently confirmed by skin biopsy. The patient was closely questioned regarding antecedent jaundice; she admitted that she might have been jaundiced as long ago as 10 years before (at age 37) and the pigmentation and pruritus had begun, insidiously, some time before 1955. The presence of esophageal varices was demonstrated on x-ray examination.

Laboratory studies at the time of this admission revealed the following values: hemoglobin level, 13.3 Gm. per 100 cc.; red blood cell count, 4,300,000 per cubic millimeter; hematocrit reading, 38%; reticulocyte count, 0.5%; white blood cell count, 3,100 per cubic millimeter; and differential count, normal. The results of the liver tests were as follows: serum bilirubin level (one minute and total), 1.3 and 3.7 mg., respectively, per 100 ml.; alkaline phosphatase level, 82 and 45 units (King-Armstrong method) on two studies; cholesterol level, 249 mg. per 100 ml.; cephalin-cholesterol flocculation, 3+; and thymol turbidity, 11 units. The total serum protein level was 7.1 Gm. per 100 ml. (albumin 3.2 and globulin 3.9). The prothrombin time was normal. The fecal urobilinogen level was 507 mg. per day. A bone marrow biopsy disclosed normoblastic hyperplasia and an increased number of megakaryocytes.

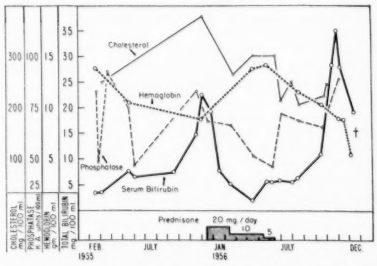

Fig. 2 (case 3).—Primary biliary cirrhosis and hypersplenism. Hemoglobin level rose and bilirubin level declined during period of treatment with steroid. Decrease in jaundice was more likely due to suppression of mild concomitant hemolytic process than to primary effect on liver. Cholesterol level was not significantly affected. Fluctuations in phosphatase levels could not be correlated with any therapeutic agent administered.

Peritoneoscopic examination was performed by Dr. J. B. Carey Jr. The liver appeared coarsely nodular and enlarged. A liver biopsy was reported by the hospital pathologist as indicating "portal cirrhosis." The patient was discharged with a clinical diagnosis of primary biliary cirrhosis and followed in the outpatient department.

The significance of the elevated fecal urobilinogen excretion in the presence of impaired excretory function on the part of the liver was not appreciated. This undoubtedly reflected an increased rate of erythrocyte destruction related to hypersplenism. The patient's condition remained virtually unchanged. Antihistaminics and lotions failed to relieve the pruritus; but except for this discomforting symptom the patient felt well. Her appetite and strength remained satisfactory, and she continued to carry out all of her household duties. In June, 1955, the patient was readmitted to the hospital for a lumbar puncture; the blood serology tests again showed positive results (V.D.R.L., + diluted; Kahn, 3+; Hinton, 4+) in May, 1955. The cerebrospinal fluid was entirely normal, and the spinal fluid (Wassermann) was negative. The treponema pallidum immobilization test, submitted to the Venereal Disease Research Laboratory in Chamblee, Ga., was reported as "nonreactive." In view of

the entirely negative evidence for syphilis, the serologic tests were considered to have given biological false-positive reactions. An L.E. clot test was negative at this time.

The physical examination at the time of the second hospital admission revealed no essential change from that observed earlier. The laboratory values remained essentially unchanged (fig. 2); the hemoglobin level had declined somewhat. Although further evidence of hemolytic activity was not sought, the effect of the congestive splenomegaly was suggestive in that the leukocyte count was 2,750 per cubic millimeter, though the differential count was normal. The platelet count was 104,000 per cubic millimeter. The patient was again discharged, and her course was followed in the outpatient department.

As shown in figure 2, the serum bilirubin level gradually rose throughout the 10 months after the patient's original investigations. In December, 1955, the patient was readmitted for the third time for reevaluation. The degree of icterus was intense. The hepatosplenomegaly was again demonstrated. The patient's only complaints were related to pruritus and mild fatigue. The values for the liver tests were similar to those obtained initially. The hemoglobin level was 9.4 Gm. per 100 ml. Evidence of mild hemolytic activity (reticulocyte counts 1.9 and 4.6%) and an elevated fecal urobilinogen level (360 mg. per day) were demonstrated. The leukocyte count was normal (5,200 per cubic millimeter), and a normal differential count was recorded. The platelet count was 184,000 per cubic millimeter.

The administration of prednisone, 20 mg. per day, was begun during this admission, and the patient was discharged on this therapy to be followed in the outpatient clinic. The icterus declined, as can be seen from the values shown in figure 2. Initially, the patient did seem to be somewhat relieved of her troublesome pruritus, although the results were not dramatic. Despite dietary salt restriction the patient experienced fluid retention while receiving steroid therapy. She complained of epigastric distress; this discomfort was only partially relieved by an antiulcer regimen. A search was made for x-ray evidence of an ulcer, but none was demonstrated. In April, 1956, the itching was again as severe as formerly, even though the degree of icterus was greatly decreased. Methyl testosterone, 10 mg. per day, was added to the regimen during May, 1956. This afforded little subjective relief but did aggravate the problem of fluid retention. In June, 1956, prednisone therapy was discontinued. During the ensuing months, several other agents were used in an attempt to relieve the pruritus. They proved ineffectual.

In November, 1955, the patient was admitted to the hospital for the fourth time. The jaundice was again intense, but in other respects the patient's general condition remained relatively satisfactory. Clear-cut evidence of hemolytic activity was obtained at this time in a study conducted by Dr. A. Sigrid Gilbertson. The half-life of the patient's chromium-tagged red blood cells was shown to be only 12 days as compared to a normal of 25 to 30 days. A splenectomy and spleen-renal anastomosis was advised. The patient requested that this be postponed until after the Christmas holidays. This seemed to be a reasonably safe request to grant in view of the apparent well-being of the patient and the chronic nature of her illness. She was permitted to return to her home in rural Minnesota.

Unfortunately the patient experienced a massive hemorrhage from esophageal varices on Dec. 26, 1956. She was subsequently returned to the University Hospital. Despite multiple transfusions and esophageal tamponade the patient continued to bleed massively and remained in a shock-like state. In desperation, an emergency operation was performed and an attempt made to ligate the bleeding esophageal varices by a transthoracic approach. The patient was in a critical condition preoperatively and failed to rally. She died the next day. An autopsy examination revealed cirrhosis, esophageal varices, splenomegaly, ascites, and bilateral hemothorax, most marked on the left side. The spleen weighed 900 Gm. and exhibited congestive changes. The liver weighed 2,540 Gm. and was deeply bile stained and nodular. The gallbladder and bile ducts were normal. Microscopic sections of the liver revealed the characteristic architectural alterations of cirrhosis. The pathologist reported a diminished number of small bile ducts in the fibrous septums. The larger intrahepatic bile ducts were not believed to be abnormal.

This case illustrates a number of features that occur in primary biliary cirrhosis. It is possible that the disease actually began some time before the patient first consulted a physician. The manifestations of the disease were well advanced when the patient was first admitted in February, 1955, since hepatosplenomegaly, pigmentation, and demonstrable esophageal varices already existed. There was suggestive evidence of a slight increase in the rate of erythrocyte destruction even then, though its significance was not appreciated. The slight elevation of the fecal urobilinogen level in a patient with evidence of impaired ability of the liver to excrete bilirubin was such an indication. The slow rise of the serum bilirubin level over a period of the next 10 months (fig. 2) reflected an imbalance between the daily pigment load and the ability of the excretory system to fully meet these demands.

In view of the complexity of such cases it is not at all surprising that the true significance of a gradually rising bilirubin level was incorrectly interpreted and the assumption made that the patient's liver function was seriously decreasing. The trial of steroid therapy was commenced in December, 1955, with the thought that this might possibly reduce the intrahepatic obstruction. In retrospect, the decrease in the serum bilirubin level that occurred between December, 1955, and June, 1956, was more likely due to a suppression of the patient's mild hemolytic activity rather than any primary effect upon the liver. Presumably, the liver was able to cope with a moderate bilirubin load but could not quite keep pace with a moderately increased work load.

The decision to advise a splenectomy and spleen-renal anastomosis should have been reached earlier. It is difficult to advocate a shunting operation as a prophylactic measure in patients with esophageal varices before an episode of bleeding has once occurred. This is especially true in patients with cirrhosis where the operative mortality is appreciable. If the patient survives the first episode of bleeding, the victim and the family are in a much better position to understand the hazards imposed by the presence of varices and the need for taking the necessary operative risk to forestall future episodes. Unfortunately the initial episode of bleeding may prove fatal, as in the case just cited.

In instances of cirrhosis and congestive splenomegaly, consideration should be given to the additional effect of hypersplenism with its attendant

hemolytic activity, leukopenia, or thrombocytopenia in the decision regarding prophylactic shunting operations. When a patient with x-ray evidences of esophageal varices exhibits signs of hypersplenism, there may be reason to adopt a bolder attitude and to advise splenectomy and spleen-renal anastomosis without waiting for the first hemorrhage to occur. Admittedly a portocaval anastomosis does effect a greater reduction in portal pressure than does a spleen-renal anastomosis, but in some cases, at least, the congestion of the spleen is not relieved rapidly after a portocaval anastomosis, and the harmful effects of hypersplenism are not promptly eradicated. In selected cases, the removal of the spleen and the performance of a spleen-renal anastomosis may be the operation of choice.

Primary biliary cirrhosis illustrates some additional clinical aspects of intrahepatic obstructive jaundice. It seems important to emphasize that icterus may not necessarily be the first manifestation of the disorder, though the diagnosis is seldom considered before jaundice does appear. In this disease the degree of elevation of serum bilirubin level does not necessarily parallel the degree of parenchymal cell damage as it usually does in other forms of cirrhosis. In such patients, a coexisting hemolytic process related to congestive splenomegaly may greatly exaggerate the degree of icterus.

Summary

The clinical features of jaundice due to intrahepatic obstruction closely simulate those of extrahepatic biliary obstruction. In most instances a correct diagnosis can be made by analyzing the data obtained by clinical, laboratory, x-ray, and histological studies. In some instances operative cholangiography may be required if, after four to six weeks of medical treatment and study, the distinction cannot be made.

Primary intrahepatic cholestasis represents one form of jaundice resulting from intrahepatic obstruction. It is usually a manifestation of a drug sensitivity phenomenon of the type seen in patients who develop reactions to arsenical drugs or chlorpromazine. The intrahepatic obstruction to bile flow is usually self-limited. In rare instances, jaundice may be protracted.

Jaundice due primarily to intrahepatic obstruction (cholestasis) rather than to hepatocellular damage is occasionally seen in patients with viral hepatitis. An experienced pathologist can usually make the correct diagnosis on the basis of a needle biopsy of the liver.

Jaundice due to intrahepatic obstruction is a prominent clinical feature of primary biliary cirrhosis. The rate of bilirubin production (i. e., rate of red blood cell destruction) must be considered in assessing the clinical significance of the degree of icterus at any given time in the course of this progressive disease.

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MECHANISMS OF BILE SECRETION

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The formation of bile in the liver is a complicated process. One group (A) of substances appears in bile in the same concentrations as in blood; this includes glucose and the chlorides of sodium and potassium. A second group (B) appears in bile concentrated as much as hundredfold; this group includes the bile salts, bile pigments, and certain test substances like sulfobromophthalein. A third group (C) is retained in the blood and appears in the bile only in very low concentrations, if at all. Groups A and B are controlled independently of each other, and substances of group B are transferred from blood to bile by an active secretory process. The transfer of sulfobromophthalein involves some active secretion, some storage, and some chemical conversion with other phenomena in addition. Since better understanding of these processes is essential to the interpretation of functional tests and the planning of treatment, further fundamental research is needed.

Bile occupies a peculiar position among secretions: It appears to be somewhere intermediate, from the point of view of its origin, between urine —the result of a sequence of filtration, reabsorption, and secretion—and milk, saliva, or other secretions which spring fully formed from the body of the cells of many typical glands. Understanding of the mechanisms of bile formation has lagged, in spite of a large volume of experimental observations, largely because the pattern of a functional anatomy of the hepatic secretory apparatus has not been established to date. Yet, I believe that enough data have accrued in recent years to justify an attempt at formulating such a picture. This communication will present the results of such an attempted synthesis together with a brief synopsis of the type of experimental material on which my model is based.

Bile is a highly complex composite secretion of widely varying composition. Sometimes this truism if lost sight of, especially in discussions of histopathological material where long-standing usage sanctions the use of the term "bile" to describe the visualization of stainable bile salts or of bile pigments. Many of the difficulties in understanding the pathophysiology of cholestasis can be traced back to this semantic difficulty.

For present purposes, the major bile constituents can be divided into three classes on the basis of the degree of concentration they experience in passage from blood to bile. Class A includes Na^+, K^+, Cl^-, and glucose, with a bile-blood concentration ratio of nearly 1.0; class B includes taurocholates, glycocholates, other bile salts, dehydrocholates, bilirubin diglucuronide, other bile pigments, sulfobromophthalein, fluorescein, rose bengal, and possibly creatinine, with a concentration ratio of 1:10 to 1:1,000; and class C includes alkaline phosphatase, inulin, sucrose, phosphates, and possibly cholesterol, phospholipids, and mucoproteins (plasma proteins, with the exception of alkaline phosphatase, appear not to be represented in the bile), with a concentration ratio of less than 1.0.

This classification can be traced back at least to the experiments of Höber and his school.[1] For the present discussion only classes A and B are relevant. They account for the water and about 95% of the dry matter of bile. Class C poses a series of intriguing but as yet largely unsolved questions and will be left out of the following discussion.

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Read in the Symposium on Modern Concepts of Intrahepatic Obstructive Jaundice before the Section on Gastroenterology and Proctology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Class A Substances

Class A substances, almost by definition, are transferred to bile in a group, and the rate of their transfer bears no necessary relation to the rate of class B compound secretion.[2] The table lists a few examples in which changes in bile flow rate or composition occur in the absence of corresponding blood composition changes, suggesting that the mechanisms of class A and of class B secretion should be considered as independent of each other in any analysis of bile secretion.

The fact that class A substances as a group appear in bile in concentrations closely reflecting those of plasma has suggested to some that a filtration reabsorption process is the basis of bile volume control. This, however, is incompatible with the experimental facts.

Thus, filtration can be ruled out because bile flow continues up to limiting pressures which, in the isolated rat liver, are always greater than blood pressures.[3] If, furthermore, one takes into account the effective colloid osmotic pressure of the plasma proteins (all but one or two minor ones of which are absent from bile), a pressure differential of such magnitude results that any filtration process can be ruled out a priori. Even a second order con-

tribution of blood pressures to bile flow rate can be ruled out, since bile flow rates are independent of blood flow or blood pressure whenever the oxygen supply to the tissue is not the limiting factor. This condition can be satisfied at fairly high rates of perfusion at body temperature [3] or over an extreme range of perfusion rates (from 0.3 to 3.0 cc. per gram of liver per minute) either at reduced temperature (30 C) or at elevated oxygen partial pressures (4 atm.).[4]

Active reabsorption also can be eliminated as a factor in bile volume regulation. Under constant blood flow conditions, cooling of the liver results in a sharp fall of bile flow rate—not a rise, as would be predicted from any mechanism dominated by reabsorption. In the rat liver, a 10 C reduction of perfusion temperature reduces bile flow rate by a factor of four between 38 and 18 C.[5] Likewise, ether anesthesia results in a reversible fall of bile flow rate. Thus, it would appear that, in essence, bile formation involves the active transfer of water and possibly of other class A substances from blood to bile.

Further light on blood-bile relations is shed by the study of such other class A components as the monovalent ions Na^+, K^+, and Cl^-. The concentrations of all of these in bile rigorously parallel their concentrations in blood plasma regardless of how much deviation from normal blood levels is seen. In rat bile, potassium concentrations exceed plasma potassium concentrations by about 15%, while sodium and chloride concentrations are very nearly equal in the two phases.[6] This equality of plasma and bile electrolyte concentrations—and osmotic pressures—is preserved even when plasma osmolarity is doubled by the addition of sodium chloride. Bile flow rate, however, is drastically reduced by such a procedure, indicating once again that a cellular phase rather than extracellular equilibrium governs bile flow rate. The location of this cellular phase is suggested in this case by the appearance of watery vacuolation in the hepatic polygonal cells.[7]

The dominant role of the hepatic cells in bile secretion is further confirmed by the observation that in many forms of toxic hepatitis, where bile suppression is among the earliest physiological manifestations, early histopathological changes are confined to these hepatic cells.[8] Thus, transfer of water to bile involves an active, energy-consuming process, is likely to be located at the level of the hepatic cells, and consequently would appear to involve of necessity the transfer of water into the bile capillaries enmeshing these cells.

Once in the biliary tree, bile is not completely isolated from the blood stream. Thus, a net transfer of fluid out of the biliary tree could be demonstrated at elevated bile pressures.[3] The rate of such backflow is dependent on bile pressure: it appears to be nil or very slow, relative to bile secretion at pressures up to about 12 cm. H_2O, and increases very rapidly with further increases in bile pressure until backflow balances secretion rate. This point is the one commonly determined in measurement of so-called bile secretion pressures. Bile composition appears to be independent of bile pressures below 10 or 12 cm. and varies at higher pressures in a manner suggesting interference with the secretory apparatus rather than concentration of bile by selective back filtration.[1] When hepatic venous pressures are elevated at constant portal pressure, it has been found in the isolated rat liver that limiting bile secretion pressures are not similarly raised but either remain constant or decrease slightly. This finding suggests that leakage of bile from the biliary tree under these conditions occurs not at the level of the sinusoidal bed but, rather, hemodynamically close to the entry of the portal blood into the liver, i. e., at the level of the portal areas or even further upstream.

Exchange of electrolytes can occur between bile in passage through the biliary tree and blood plasma. This follows in particular from studies of bile potassium: after radioactive potassium (K^{42}) injection into the blood stream, the specific activity of the large hepatic intracellular potassium pool

Examples of Independent Variability of Secretion into Bile of Class A and Class B Components

	Condition	BSP Secretion Rate	Taurocholate Concentration	BSP Concentration Maximum	Bile Flow Rate
Dog (BSP infusion)	Breathing actively	1.30 mg./min.	...	...	98 microliters/min.
	Diffusion respiration (2.5 atm. O_2)	1.07 mg./min.	...	...	38 microliters/min.
Rat (isolated liver)	During 1st hr. of perfusion	...	2.3 mg./cc.	...	1.2×10^{-2} cc./min.
	During 3rd hr. of perfusion	...	0.25 mg./cc.	...	1.0×10^{-2} cc./min.
Rat (isolated liver; 3 mg. of BSP injected)	38 C	...	...	94 mg./cc.	1.5×10^{-2} cc./min.
	30 C	...	...	97 mg./cc.	0.42×10^{-2} cc./min.
Rat (isolated liver)	During steady state	95 meq./min.	...	...	2.2 cc./min.
	In spontaneous failure	85 meq./min.	...	...	0.50×10^{-2} cc./min.
Dog (bile fistula)	Continuous BSP (or penicillin) infusion at various rates	BSP (or penicillin) "clearance" rate decreasing sharply with increasing plasma BSP concentration			
	Sodium or lithium chloride by continuous infusion at various rates	Sodium or lithium "clearance" independent of plasma sodium or lithium concentrations			

rises somewhat gradually while bile potassium specific activity has reached the values prevailing in plasma within about one minute.[4] Bile potassium thus is derived from blood and not from the cellular phase of the hepatic parenchyma. The rate of K^{42} appearance, furthermore, suggests that this ion entered the biliary tree pretty well downstream rather than in the canalicular headwaters. Similar results, though less sensitive because of the small sizes of intracellular stores, have been obtained for Na^+ and Cl^-. Together with the above data on the origin of the biliary fluid phase, these data, then, provide the basis for the conclusion suggested above that bile secreted by the hepatic cells in passage down the biliary tree is afforded an opportunity to reach electrolyte equilibrium with the blood plasma. It is tempting to assign this process to the small bile ducts and ductules with their investing vascular plexuses.[9]

Class B Substances

In contrast with class A bile components, those of class B appear in bile in such concentrations that there can be no doubt about the fact that an active secretory process of some kind must be involved in the transfer from blood to bile. Class B compounds share a number of chemical characteristics: they are usually organic carboxylic acids or their salts of molecular weights of the order of 300 or greater, and they share a marked tendency to form complexes with plasma proteins, particularly with plasma albumin. With respect to secretion into bile, also, there are many similarities between these substances, although quantitative differences may exist between them with respect to the degree to which particular properties are displayed. Sulfobromophthalein sodium, an exogenous dye, has had perhaps more study than any other compound from the point of view of its fate in relation to bile secretion. Since, wherever they have been checked, conclusions derived from the study of sulfobromophthalein secretion correspond with observations for other class B compounds, attention here will be focused on this substance as a prototype of the entire class.

Sulfobromophthalein is secreted into bile at concentrations that always far exceed those in the blood stream. Characteristically, however, there is a limiting rate of dye secretion beyond which increasing the dose or the infusion rate of sulfobromophthalein no longer affects the secretion rate; the mechanism involved, whatever its nature, appears to be saturated.

Similar saturation phenomena have been seen for sodium dehydrocholate, bilirubin, and fluorescein[7] and would appear to be characteristic of the biliary secretion of class B compounds in general. Related to this property may well be that of competition for uptake and excretion by the liver, a phenomenon well recognized for the pair dehydrocholate and sulfobromophthalein[10] and recently described also for other pairs, such as bilirubin and sulfobromophthalein and bilirubin and bile salts.[7] A similar mechanism may underlie the inhibition of sulfobromophthalein uptake in the presence of probenecid (Benemid) and of certain shellack suspensions.[7] There is a suggestion in these data that uptake—that is, blood to secretory cell transfer—rather than secretion into bile is involved in these mutual inhibitions.

The path of class B compounds from blood to bile has been explored visually, by tracer methods, and physiologically. By visual observation of fluorescein secretion, Hanzon has demonstrated a sequence of uptake into parenchymal cells, secretion into bile canaliculi, and transport down the biliary tree for this dye.[7] Tracer studies involving sulfobromophthalein labeled with radioactive sulfur (S^{35}) have confirmed and expanded this picture. In the first place, they have proved that blood to bile transport of sulfobromophthalein must involve a cellular phase. Bile in several species does not contain sulfobromophthalein as such but, rather, a series of sulfobromophthalein derivatives together with traces of sulfobromophthalein only.[11] The conversion does not take place in the blood stream, for blood contains mere traces of these sulfobromophthalein derivatives over most of the course of sulfobromophthalein excretion, and the hepatic parenchyma is very active in effecting the conversion. The end product of sulfobromophthalein metabolism in the rat is a phthalein dye, provisionally designated as sulfobromophthalein II, which is secreted without further conversion into bile. The fact that blood-to-bile concentration ratios for this dye, too, are always considerably below 1:1, ranging around 1:10 to 1:50 during continuous infusions in the isolated rat liver, conclusively proves that chemical conversion is not essential to uphill secretion of class B compounds into bile.

Transfer of sulfobromophthalein from blood to bile is not a simple a-to-b process. Even at subsaturation doses, as much as half of the dye entering the cells is stored away.[12] The site of storage appears to be the hepatic cell, both from analogy with fluorescein and on the basis of radioautographic studies. The stored dye is eventually available for excretion into bile. However, maintenance of high secretion rates depends on continued delivery of sulfobromophthalein or of its derivatives to the liver via the blood stream: transferring an isolated liver loaded with sulfobromophthalein or sulfobromophthalein II from the dye-containing circulation to a fresh, sulfobromophthalein-free circulation results in a rapid falling off of dye con-

centrations in the bile. This behavior is in line with the mode of action of the inhibitors of sulfobromophthalein handling mentioned above.

If S^{35}-labeled sulfobromophthalein II is used in the first and ordinary sulfobromophthalein in the second circulations of such perfusion experiments, the falling off in the rate of excretion of stored up S^{35}-labeled dye after the transfer is virtually the same as though no dye were present in the second system, suggesting that stored sulfobromophthalein and freshly delivered sulfobromophthalein are secreted independently at these dosage levels. That storage and secretion of sulfobromophthalein are somewhat independent processes can also be observed in toxic liver injury; here, secretion of sulfobromophthalein is severely impaired,[12a] while storage remains effective as shown both by direct analysis[12a] and, for the damaged cells, by histological methods.[13] Similarly, in the chick embryo hepatic storage and chemical conversion are demonstrable several days before biliary sulfobromophthalein excretion.[14]

Thus, a complex picture of sulfobromophthalein handling in the liver is gradually emerging, incorporating a storage phase, possible chemical conversion, and secretion as its elements. Anatomic counterparts to these at present can only be derived by analogy with the results of direct observation of fluorescein. As before for water transfer, the parenchymal cell appears to emerge as the central secretory element for class B substances. Rigorous proof of this, however, remains to be furnished.

If the hepatic cell is the primary agent of sulfobromophthalein secretion, the dye thus secreted is delivered into the bile canaliculi which invest the hepatic cells. This conclusion once again is in agreement with Hanzon's in vivo microscopic observations.[7] In passage down the biliary tree, the sulfobromophthalein-laden bile must traverse the zone where plasma-bile equilibration occurs with respect to sodium, potassium, and chloride. In the case of class B substances, however, the rate of exchange must be far slower, since otherwise the very large concentration gradients between blood and bile could not be maintained. Possible evidence for the existence of such exchange may be found in the gradual appearance in plasma of biliary sulfobromophthalein derivatives after sulfobromophthalein injection. In bile stasis, far greater back-transfer is seen both in the blood and in liver lymph,[7] together with recycling which results in accumulation of the end product of sulfobromophthalein metabolism—sulfobromophthalein II in the rat—in the blood and liver; this, however, could represent bulk regurgitation rather than diffusion exchange. The difference in rate of exchange between sulfobromophthalein and similar compounds on the one hand and of K^+ or Cl^- on the other can be reproduced in simple collodion bag dialysis experiments, where the rate constant for sulfobromophthalein exchange is less than one-tenth as fast as that for Cl^- or K^+ exchange at concentrations comparable to those in plasma and bile. Thus, when in a typical experiment sulfobromophthalein concentration inside the bag had decreased from 100% to 80% of the initial value of Cl^- exchange was 92% complete.

Hypothermia affects sulfobromophthalein secretion rates to about the same extent as bile flow.[4] Elevated bile pressures fail to affect bile sulfobromophthalein concentrations until levels are reached where bile backflow assumes important proportions; in that region bile sulfobromophthalein levels may decrease below normal for a given dose. Both these lines of observation confirm the view that selective reabsorption is not a factor in establishing sulfobromophthalein concentrations in bile.

I would like to mention two alternative points of view on sulfobromophthalein handling in the liver. Kupffer's cells were once considered involved in this process on the basis of the effect of India ink on sulfobromophthalein clearance.[15] More recent work has resolved this experiment by the demonstration that something in the suspension medium (the shellack, on most recent evidence) rather than the so-called RE blocking colloid is at the base of the effect and that loading of Kupffer's cells with inert colloid fails to modify sulfobromophthalein handling in the liver.[16]

Again, a most interesting point of view was proposed on the basis of the demonstration of an extensive peribiliary vascular plexus supplied by the hepatic artery; it was proposed that this was an expression of a major functional role of the bile ducts and that this role was the secretion of important bile components, including sulfobromophthalein.[17] As far as the latter assertion is concerned, direct check with use of simultaneous injection of sulfobromophthalein into the portal vein and of S^{35}-labeled sulfobromophthalein into the hepatic artery of dogs has shown either that there are no route-dependent differences in secretion of dye or that the dye introduced into the portal vein is actually secreted preferentially. Thus, the bile ducts do not appear to play a predominant active role in sulfobromophthalein secretion.[18] The peribiliary plexus would, however, appear to be an excellent anatomic device for effecting the exchange between blood and bile constituents described in preceding sections of this paper.

Comment

The following concept represents a useful working hypothesis of the mechanism of bile secretion: Bile flow is initiated by the secretory activity of the

hepatic cells. Since, at present, no other single bile component appears to be linked with this process, it seems useful to consider this process as water secretion. Substances of class B are transferred from blood to bile by the same hepatic cells, forming a primary bile in the bile canaliculi.

Primary bile, in passage down the biliary tree, comes into restricted contact with blood plasma. This results in equilibration of Na^+, K^+, and certain other ions and may result in a limited loss from bile of class B components. The difference in exchange rates seems to be largely due to differences in diffusion rates in solution and to differences in ionic radii in relation to the effective pore sizes of the membranes separating blood and bile.

Bulk transfer of bile from the biliary tree to the blood stream can occur when bile pressures are raised. Under such conditions, as well as in the normal liver, selective retention in bile of specific components appears to be of minor importance in determining bile concentration. Anatomically, the peribiliary vascular plexus may represent the area of blood-bile exchange and the juxtasinusoidal extensions of the bile canaliculi,[19] as well as the ductular region,[7] appear likely sites for bulk backflow.

Conclusions

The physiological anatomy of bile secretion, as has been proposed, must be subjected to much further experimental work along such promising lines as the analysis of liver lymph composition, the effects of intermittent or of relative bile stasis, and the ontogeny of bile secretion and its relation to the biochemical and morphological development of the liver. At the same time, I feel that enough background is available to justify preliminary turning of attention to the basic mechanisms which convert the energy provided by biochemical reactions to the physical work of bile secretion. A beginning in this direction has been made in oxygen tension–bile flow studies, in the exploration of enzyme inhibitor effects on bile flow and of the biochemical effects of certain hepatotoxins, in attempts to correlate nutritional studies and bile secretion, and, in particular, in the exploration of the intriguing variety of effects of the several bile flow–stimulating or choleretic agents. This, however, is another tale which, I hope, can be considered in a future discussion.

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CLINICAL NOTES

PERSISTENT SUBARACHNOID-PLEURAL SPACE FISTULA

REPORT OF A CASE

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A fistulous connection between the subarachnoid space of the spinal canal and the pleural space is evidently a rare pathological entity. We have been unable to find a previous account of this condition in the literature. We feel, therefore, that the following case report should be of interest.

A 19-year-old paraplegic man was admitted to the Chicago State Tuberculosis Sanitarium on Oct. 31, 1955, because of a right pleural effusion. The history revealed that he had had no significant illness until 1952, when he received a thoracoabdominal gunshot wound. This wound made an emergency exploratory laparotomy necessary and also was the cause of his present paraplegia. Since the onset of paraplegia he had developed chronic urinary tract infection and decubitus ulcers.

Examination revealed paraplegia of the lower extremities and skin anesthesia from the level of the 10th thoracic segment down. There was a surgical scar on the upper part of the abdomen and a bullet could be palpated in the subcutaneous tissues of the back, near the midline, at about the level of the sixth thoracic vertebra. Breath sounds were impaired in the right lung base.

On Oct. 2, 1955, the patient had developed the pleural effusion while in another hospital. This occurred six weeks after intraspinal alcohol injection, which was given in an attempt to convert the paraplegia from the spastic to the flaccid type. At thoracentesis, 1,800 cc. of clear fluid was obtained. The pleural fluid was negative bacteriologically. The Mantoux test (with purified protein derivative) gave a positive finding in second strength.

Even though there was no bacteriological confirmation of a tuberculous cause, the patient was placed on therapy with streptomycin, aminosalycilic acid, and isoniazid. After eight months of treatment with these drugs, the patient continued to form fluid at a rate requiring removal of 1,000 to 1,500 cc. every two or three weeks. All bacteriological studies of this fluid, including guinea pig inoculations, continued to show negative results. The specific gravity of the fluid was 1.010, the cell count varied from 1 to 3 per cubic millimeter, and the total protein content varied from 1.25 to 1.83 Gm.%. Total cholesterol level was 22 mg.%.

At thoracotomy, 3,500 cc. of straw-colored fluid was removed from the right side of the chest. The pleura was completely normal in appearance except for adhesions along the bullet tract. This appearance was baffling until a minute, dimple-like defect was found in the pleura on the lateral surface of the vertebral column which was exuding small amounts of clear fluid. This defect was probed and found to be a fistulous tract which passed toward the posterior portion of the seventh thoracic vertebra. This tract was unroofed to the point of its termination in the spinal canal, where a small perforation in the dura was discovered. The dura was opened sufficiently to inspect the cord and to make sure no foreign body was present. The dura was then closed with fine silk, and flaps of intercostal musculature and pleura were brought across the site of the fistula to help obliterate it. The parietal pleura was then stripped in the gutter and lateral chest wall to insure subsequent pleural symphysis.

Postoperatively, the patient complained of headaches for about six weeks. This symptom was relieved by lumbar puncture on one occasion. These headaches gradually subsided, and the patient was returned to his original hospital. He has had no recurrence or subsequent complications in a follow-up period of one and one-half years.

Comment

We have presented the case of a paraplegic youth who developed a pleural effusion three years after a gunshot wound which caused his paraplegia. The offending bullet had apparently traversed the right side of the chest, vertebral column, and spinal canal. The pleural effusion developed six weeks after an intraspinal alcohol injection. It was at first presumed to have a tuberculous origin, but after an adequate period of antituberculosis therapy the effusion did not subside and exploratory thoracotomy was performed. This revealed the presence of a fistula between the pleural and subarachnoid spaces.

We are unable to account for the three-year interval between the gunshot wound which produced the fistulous tract and the onset of the effusion. Although the alcohol injection seems to be the only significant event associated with the appearance of the effusion, a causal relationship is not clear.

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BLOOD DYSCRASIAS ASSOCIATED WITH TOLBUTAMIDE THERAPY

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During the three years of its use, tolbutamide has established a remarkable record for safety. Side-reactions have been relatively few, consisting of mild gastrointestinal disturbances, skin eruptions, and mild granulocytopenias.[1] These reactions are generally not serious and disappear either after discontinuation of use of the drug or in spite of its continued administration. To date, no serious untoward reactions have been reported. Reactions, however, do occur. It should not be surprising, therefore, if an occasional case should assume grave proportions. With this thought in mind, a case is reported in which serious depression of the bone marrow was observed during the course of treatment with tolbutamide.

Report of a Case

A 69-year-old man was admitted to St. Vincent's Hospital on Aug. 7, 1956, with the chief complaint of weakness and collapse. The history revealed that in 1940 he was hospitalized for rectal abscess and in 1942 for cellulitis of the legs. In 1950, he was found to be hypertensive and suffering from obliterative arteriosclerosis and varicose veins with intermittent claudication. In 1951, a saphenous vein ligation was done; three months later, a sympathectomy on the left side was performed. In 1952, sympathectomy was done on the right. In 1954, he began to suffer from angina pectoris.

Diabetes was detected in 1939 when he was hospitalized for treatment of a rectal fistula. There were no symptoms of diabetes. The diabetes was treated with diet alone for the first year; thereafter, 30 to 35 units of protamine zinc insulin was taken daily. Control of diabetes had been poor due to lack of cooperation. Two years prior to the present illness, the patient changed his attitude and paid close attention to his diet and insulin dosage. Since then, control has been excellent, as manifested by almost normal blood sugar levels, minimal glycosuria, and freedom from hypoglycemic reactions. The weight remained stable. Several blood cell counts during this period were either normal or showed mild degrees of anemia attributed to rectal bleeding from hemorrhoids.

On May 29, 1956, the fasting blood sugar level was 132 mg.%; the urine showed a trace of albumin but no sugar or acetone. His weight was 164 lb. (74.4 kg.). The patient was well and asymptomatic. Therapy with protamine zinc insulin was discontinued.

On June 5, 1956, the fasting blood sugar level was 211 mg.%. A mild postprandial glycosuria was recorded, but acetone was not present. His weight was 159 lb. (72.1 kg.). The patient felt well and was asymptomatic. No insulin was recommended.

History of Present Illness.—On June 19, 1956, the fasting blood sugar level was 279 mg.%; a moderate glycosuria was noted throughout the day but no ketonuria. The patient's weight was 157 lb. (71.2 kg.). He had no symptoms and no complaints. A blood cell count was ordered, and the patient was placed on tolbutamide therapy, 1 Gm. before breakfast and supper. No report on the blood cell count was received.

On June 26, 1956, the fasting blood sugar level was 127 mg.%; there was mild postprandial glycosuria. His weight was 156 lb. (70.8 kg.). There were no signs of hypoglycemia, no symptoms, and no complaints. The evening dose of tolbutamide was reduced to 0.5 Gm.

On July 10, 1956, urine findings were unchanged. The fasting blood sugar level was 162 mg.%. The patient looked and felt well but complained of mild exertional angina in the morning. Tolbutamide dosage was increased to 1 Gm. given twice daily.

During the following weeks, the patient did not return for weekly check-ups as was advised. When he appeared again on Aug. 7, 1956, he was pale. He reported that for three weeks he had felt weak and had collapsed several times. He blamed the tolbutamide for his symptoms and stopped taking it, but he did not resume insulin therapy. When he did not notice any improvement, he returned to the clinic.

The urine showed glycosuria but no ketonuria. He was admitted to the hospital. Physical examination showed his weight to be 154 lb. (69.9 kg.), temperature 98 F (36.6 C), pulse 80 per minute and irregular, blood pressure 140/76 mm. Hg, and respiration rate 20 per minute. The lungs showed crepitant rales at both bases. The heart was slightly enlarged, and a faint systolic murmur was heard over the apex. There were operative scars on the lower extremities. The feet were cool, and the pedal pulses were not palpable. The tendon reflexes were absent in the lower extremities. Chest x-ray showed cardiac enlargement, pulmonary congestion, and a small pleural effusion on the right side. The electrocardiogram showed atrial fibrillation with a left ventricular strain pattern. The blood cell count was as follows: hematocrit value, 20%; hemoglobin level, 5.8 Gm.%; red blood cell count, 2,300,000 per cubic millimeter; and white blood cell count, 2,200 per cubic millimeter, with reticulocytes 0.6%, polymorphonuclears 43%, lymphocytes 48%, monocytes 4%, and platelets 80,000 per cubic millimeter. Bone marrow revealed sparsely cellular marrow with relative hypoplasia of the myeloid and relative hyperplasia of the erythroid series.

The patient was given blood transfusions. The diabetes was promptly controlled with diet and insulin and the cardiac decompensation corrected with digoxin and diuretics. Attempts to improve the blood dyscrasia with vitamin B_{12}, liver extract, iron, and steroids were unsuccessful. The patient was kept comfortable by repeated transfusions. He was discharged on Aug. 29, 1956, and advised to return at stated intervals for reevaluation. Repeated bone marrow examinations were done during his stay in the hospital but revealed no significant change.

The patient was readmitted to the hospital on Sept. 11, 1956. Except for the absence of congestive failure the physical findings were unchanged. The vital signs were normal. The laboratory data revealed blood urea nitrogen level, 20 mg.%; creatinine level, 2.5 mg.%; hemoglobin level, 6.4 Gm.%; red blood cell count, 2,400,000 per cubic millimeter; and white blood cell count, 2,600 per cubic millimeter, with polymorphonuclears 40%, eosinophils 2%, monocytes 1%, lymphocytes 57%, and platelets 61,000 per cubic millimeter. Repeated blood cell counts at weekly intervals revealed no significant changes.

The patient was given blood transfusions. A second trial with the above-mentioned hematinics proved equally unsuccessful. The patient remained fairly comfortable until Oct. 9, 1956, when he experienced a moderate sustained fever and signs of pneumonia at both lung bases. Tetracycline (Achromycin) was given, and the temperature returned to normal after four days. On Oct. 16, 1956, the patient, while sitting quietly in a chair, suddenly fell over and died.

Autopsy was performed on Oct. 18, 1956, by Dr. Julia Miyares. A brief summary of the findings is as follows: arteriosclerotic heart disease with coronary artery sclerosis; segmental narrowing and subintimal hemorrhage of the left anterior descending coronary artery; and subendocardial and subepicardial petechiosis of the myocardium. The lungs showed confluent lobular pneumonia, involving the right

From St. Vincent's Hospital.

middle and left lower lobe with a small caseous tubercular focus in right upper lobe. The pancreas was the site of mild hemorrhagic peripancreatitis. The bone marrow revealed marked hypoplasia of the granulocytic, megakaryocytic, and erythroid series. The features were those of severe hypoplasia.

Comment

It may well be said that conclusive proof for causal connection between tolbutamide therapy and the blood dyscrasia has not been established since there is no record of a blood cell count immediately preceding use of the drug. Against this contention, however, are the following facts: For quite some time before and for at least three weeks after the use of tolbutamide, the patient felt well, looked his usual self, and had no complaints except that of occasional mild angina, which he had been having for over two years. Search of his records for over four months prior to his anemia failed to reveal any suggestive complaints or use of other medication. The patient himself denied taking any medicine, nor could any history be elicited that indicated exposure to other toxic agents. The patient's history and the blood findings in August, 1956, are compatible with the suggestion that the onset of the dyscrasia occurred shortly after the beginning of the use of tolbutamide. Certainly, the consideration of the possibility of a causal connection between the drug and blood findings appears justified.

Summary and Conclusions

Severe, protracted, and probably lethal aplastic anemia occurred in a patient taking tolbutamide. This should in no way discourage the use of this effective and generally remarkably safe drug. It should, however, remind the physician of the possibility that mild and inconsequential reactions may occasionally assume grave proportions and alert him to the necessity of detecting them by frequent blood cell counts early in the course of treatment.

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LEG ULCER IN RHEUMATOID ARTHRITIS

Louis W. Granirer, M.D., Jamaica, N. Y.

Rheumatoid arthritis has many visceral manifestations which serve to emphasize the systemic nature of the disease. Lesions have been reported in the nerves, muscles, heart, brain, eye, bones, gastrointestinal tract, pleura, lungs, and larynx.[1] This paper presents the clinical and histological findings in a patient with a leg ulcer in rheumatoid artritis.

Report of a Case

A man, aged 52, was admitted to the Arthritis Clinic on Feb. 2, 1957, with a history of rheumatoid arthritis since 1946. He was thin and pale. The hip joints, right knee, ankles, and right elbow and wrists were swollen and tender. The adjacent muscles were conspicuously wasted. The proximal interphalangeal joints showed characteristic "spindling" deformities, and the fingers were deviated to the ulnar side. There was a poor response to therapy with gold salts, prednisone, prednisolone, and triamcinolone in large doses. Facial roundness was evident, and he had a palpable spleen. The blood hemoglobin level was 11 Gm. per 100 cc.; the white blood cell count was 4,200 per cubic millimeter, with 65% polymorphonuclear neutrophil leukocytes; and the erythrocyte sedimentation rate (Westergren) was 55 mm. in the first hour. The latex fixation test gave a positive result. The serum uric acid level was 2.5 mg. per 100 cc. The L. E. cell test and Wassermann test showed negative results. The temperature was 99 F (37.2 C) and blood pressure, 130/90 mm. Hg. The heart showed a moderate degree of left ventricular hypertrophy. Subcutaneous nodes (3 cm. in diameter) were found over both olecranon processes.

From the Arthritis Clinic and Department of Medicine, Queens General Hospital.

In April, 1957, he suddenly developed a painful ulcer in the posterior lower third of the right leg. It measured 4 by 5 cm. and was 0.5 cm. in depth (fig. 1). The ulcer was similar to those previously reported.[2] The margins were sharply demarcated with a typical punched-out appearance. There was little discharge, with minimal inflammatory reaction in the surrounding tissue. A greyish exudate was evident at the base of the ulcer. The pain was very distressing. My interest was intensified by the fact that this lesion did not respond to routine and accepted measures of therapy. There was no evidence of varicosities, no deep or superficial venous thrombosis, no diabetes mellitus, no evidence of infection, and no edema. Repeated cultures showed no pathogenic organisms. Complete bed rest with elevation of the foot of the bed had no effect. Prolonged local and general antibiotic therapy, steroids, gold salts, phenylbutazone, trypsin (Parenzyme), streptokinase-streptodornase (Varidase), ultraviolet rays, sulfonamides, and flexible adhesive bandage were unsuccessful.

A specimen of tissue from the ulcerated area showed three distinct features: a zone of necrosis and fibrinoid alteration; an intermediate zone characterized by palisading of histiocytes and young fibroblasts with infiltration of small round cells; and an outer zone of fibrous tissue with numerous blood vessels (fig. 2). These histological characteristics are in accord with the typical lesion of the rheumatoid nodule described by Klinge [3] in 1933 and are considered to be pathognomonic.

With large doses of methylprednisolone, this patient experienced a dramatic relief from pain and stiffness as well as a decrease in all the objective signs of joint disease. The subcutaneous nodules rapidly lost their tenderness and diminished in size. Withdrawal of the drug was followed by a rapid increase in the size and tenderness of the subcutaneous nodules. The leg ulcer, however, demonstrated no change during steroid therapy. This feature has been previously recorded in similar patients and was of considerable interest.[2]

Comment

Although rheumatoid disease has previously been described in practically all of the viscera, the precise site and the histological appearance of the leg ulcer has not been clearly defined. In a recent report of 200 leg ulcers, 150 were classified as varicose, 30 as post-thrombotic, and 20 as miscellaneous.[4]

Edema was considered to be the final cause in all three groups. The edema was due to the failure of weakened or poorly used calf muscles to maintain an adequate venous return (e. g., hemiplegia, rheumatoid arthritis, arthritis of hip and knee).

The leg ulcer reported here was very painful and was not relieved by rest. It presented a typical punched-out appearance with very little drainage. It occurred in the lower third on the posterior aspect of the leg and did not respond to conventional therapy. (The original hypothesis of edema as the cause did not provide a satisfactory explanation.)

Not all patients with rheumatoid arthritis develop leg ulcers. It is plausible that trauma may play an important etiological role. Two ulcers of this type have been observed to heal with no specific type of therapy.

Whether the connective tissue is a prime reactor in rheumatoid disease or is involved secondarily, Gross [5] believes that the crippling deformities and much of the functional impairment result from failure of the newly forming connective tissue to reproduce the normal structures. Although this healing phase may be nonspecific, it is a major feature of the course and ultimate consequence of this disease. In his opinion, there is little evidence as yet that collagen is involved in any way other than as an innocent bystander or in the healing of accompanying injury. Fibrinoid has long been considered the hallmark of connective tissue diseases and yet may be nothing but the end-result of a relatively nonspecific process. It may be recalled that the cause and cure of scurvy, a connective tissue disease, are known, but the biochemical functions of vitamin C are still unknown.[5]

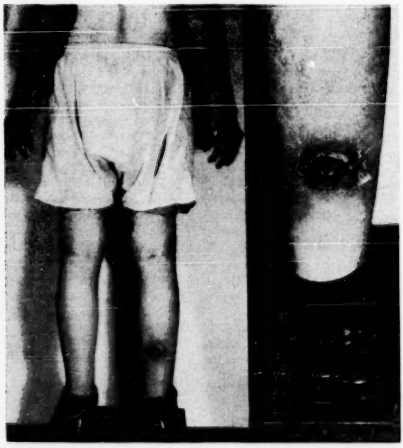

Fig. 1.—Leg ulcer in patient with rheumatoid arthritis.

Fig. 2.—Section demonstrating characteristic features of rheumatoid nodule from leg ulcer. *Left to right*, zone of fibrinoid alteration and necrosis, palisading of mesenchymal cells, and outer zone of cellular reaction.

Summary

The clinical and histopathological changes in a patient with rheumatoid arthritis with a leg ulcer were of considerable interest. Specimens of tissue from the ulcer revealed the typical rheumatoid nodule. The lesion did not disappear with any routine therapy, including that with large doses of corticosteroids. The clinical course in a case previously observed followed a similar pattern.

90-36 149th St. (35).

Dr. G. Silverman did the biopsy studies and M. Pikuritz supplied the illustrations.

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SPECIAL ARTICLE

HISTORY OF THE SECTION ON OBSTETRICS AND GYNECOLOGY OF THE AMERICAN MEDICAL ASSOCIATION

Woodard D. Beacham, M.D., New Orleans

I am grateful for the honor of your addition of my name to the roster of obstetricians and gynecologists who have occupied the chairmanship of this section, and I appreciate the opportunity of presiding at its 94th meeting. I was tempted to prepare a Chairman's address concerning the misuse of words in our discipline. For example, when one really means "nullipara" he should not say "primipara." However, consideration of philosophical subjects and reports of progress in our specialty required me to seek a complete list of the titles of addresses of my predecessors. When it became evident that no such record was available, the title chosen offered its challenge.

1847 to 1876

At the first meeting of the American Medical Association in May, 1847, in Philadelphia, Nathaniel Chapman served as President. In that year Sir James Simpson introduced chloroform anesthesia in obstetrics, Semmelweis demonstrated the role of antisepsis in the prevention of puerperal fever, and Carl Ludwig invented the kymograph. Six years prior Oliver Wendell Holmes had written his paper on puerperal sepsis.

At the meeting held a year later in Baltimore, the Committee on Obstetrics reported "the anesthetic agents ether and chloroform have now been used in perhaps 2,000 cases of midwifery, and so far as the committee have been able to learn without a single fatal, and few, if any, untoward results."

In 1859 a Section on Practical Medicine and Obstetrics was authorized following a report introduced by J. B. Lindsley of Tennessee, who was chairman of the committee appointed to inquire into the propriety of dividing the Association into sections for the better performance of its work (see table).

The 1860 meeting of the Section on Practical Medicine and Obstetrics was called to order by N. S. Davis, of Chicago, and Amos Nourse was elected the first Chairman of the Section. In his A. M. A. presidential address, Henry Miller brought out openly the question of illegal abortion and urged action by legislatures in every state against this practice. The 1861 and 1862 meetings were canceled because of the Civil War. The following year there was a meeting in Chicago without sections.

In 1864 the A. M. A. met in New York City without Southerners and Nathan Smith Davis, founder of the A. M. A., was elected President. Fordyce Barker, who was Chairman of the Section on Practical Medicine and Obstetrics, later became the first President of the American Gynecological Society. The Secretary wrote: "several hundred members being present during the course of the meeting." Papers read included "Death from Air in the Circulation Introduced Through the Uterine Sinuses"; "A Modified Ring Pessary for the Treatment and Cure of Anteflexion and Anteversion of the Uterus"; "On the Use of Pessaries"; and "The Relations of Female Patients to Hospitals for the Insane: The Necessity on Their Account of a Board of Consulting Physicians to Every Hospital."

At the third meeting Zina Pitcher, who served as the 10th President of the A. M. A. and was thrice mayor of Detroit, occupied the chairmanship. H. R. Storer, of Boston, was awarded the A. M. A. gold medal for his essay entitled "The Criminality and Physical Evils of Forced Abortions." In the Section's minutes it is recorded that the Secretary commenced to read the paper of an absent member and, after the expiration of more than an hour, a motion was made to suspend its further reading and it was referred to a committee.

The program of the fourth annual meeting contained no obstetrics. There was a "Report of the Committee on Diphtheria as It Has Occurred in the United States" and one on "So-called Spotted Fever."

At the 1867 session the designation was the Section on the Practice of Medicine and Obstetrics. Included in the program was a paper entitled "Extra-uterine Foetation and Gestation, and the Early Signs Which Characterize It: Symptoms of the Fatal Hemorrhage into the Peritoneal Cavity, Its Usual Termination: Suggestions for the Positive Diagnosis of This Fatal Condition, and a Plan for the Treatment Indicated in It, with a View of

From the Department of Obstetrics and Gynecology, Tulane University School of Medicine.

Chairman's address, read before the Section on Obstetrics and Gynecology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Meetings of the Section

Place	Year	Chairman
Louisville, Ky.	1859	Section on Practical Medicine and Obstetrics authorized
New Haven, Conn.	1860	Amos Nourse, Maine
	1861	Meeting canceled because of war
	1862	Meeting canceled because of war
Chicago	1863	No section meetings
New York	1864	Fordyce Barker, New York
Boston	1865	Zina Pitcher, Detroit
Baltimore	1866	Lake I. Tefft, Syracuse, N.Y.
Cincinnati	1867	M. K. Taylor, Keokuk, Iowa
Washington, D. C.	1868	R. R. McIlvaine, Cincinnati
New Orleans	1869	H. F. Askew, Wilmington, Del.
Washington, D. C.	1870	Joseph Kammerer, New York
San Francisco	1871	H. R. Storer, Boston
Philadelphia	1872	D. A. O'Donnell, Baltimore
St. Louis	1873	Zina Pitcher, Detroit
Detroit	1874	Theophilus Parvin, Indianapolis
Louisville, Ky.	1875	W. H. Byford, Chicago
Philadelphia	1876	S. C. Busey, Washington, D. C.
Boston	1877	James P. White, Buffalo
Buffalo	1878	E. W. Jenks, Detroit
Atlanta, Ga.	1879	E. S. Lewis, New Orleans
New York	1880	Albert H. Lewis, Bradford, Pa.
Richmond, Va.	1881	James R. Chadwick, Boston
St. Paul	1882	H. O. Marcy, Boston
Cleveland	1883	J. K. Bartlett, Milwaukee
Washington, D. C.	1884	Thaddeus A. Reamy, Cincinnati
New Orleans	1885	R. S. Sutton, Pittsburgh
St. Louis	1886	S. C. Gordon, Portland, Maine
Chicago	1887	F. M. Johnson, Kansas City, Mo.
Cincinnati	1888	Ely Van De Warker, Syracuse, N.Y.
Newport, R. I.	1889	W. H. Wathen, Louisville, Ky.
Nashville, Tenn.	1890	William Warren Potter, Buffalo
Washington, D. C.	1891	Chas. A. L. Reed, Cincinnati
Detroit	1892	E. E. Montgomery, Philadelphia
Milwaukee	1893	John Milton Duff, Pittsburgh
San Francisco	1894	Jos. Eastman, Indianapolis
Baltimore	1895	F. H. Martin, Chicago
Atlanta, Ga.	1896	Joseph Taber Johnson, Washington, D.C.
Philadelphia	1897	Milo B. Ward, Topeka, Kan.
Denver	1898	Joseph Price, Philadelphia
Columbus, Ohio	1899	A. H. Cordier, Kansas City, Mo.
Atlantic City, N. J.	1900	W. E. B. Davis, Birmingham, Ala.
St. Paul	1901	Henry P. Newman, Chicago
Saratoga Springs, N. Y.	1902	J. H. Carstens, Detroit
New Orleans	1903	A. Palmer Dudley, New York
Atlantic City, N. J.	1904	L. H. Dunning, Indianapolis
Portland, Ore.	1905	C. L. Bonifield, Cincinnati
Boston	1906	C. S. Bacon, Chicago
Atlantic City, N. J.	1907	J. Wesley Bovee, Washington, D.C.
Chicago	1908	Walter B. Dorsett, St. Louis
Atlantic City, N. J.	1909	W. P. Manton, Detroit
St. Louis	1910	John G. Clark, Philadelphia
Los Angeles	1911	H. G. Wetherill, Denver
Atlantic City, N. J.	1912	C. Jeff Miller, New Orleans
Minneapolis	1913	F. F. Simpson, Pittsburgh
Atlantic City, N. J.	1914	E. Gustav Zinke, Cincinnati
San Francisco	1915	Thomas S. Cullen, Baltimore
Detroit	1916	Edward Reynolds, Boston
New York	1917	Howard W. Longyear, Detroit
Chicago	1918	Brooke M. Anspach, Philadelphia
Atlantic City, N. J.	1919	Thomas J. Watkins, Chicago
New Orleans	1920	Reuben Petersen, Ann Arbor, Mich.
Boston	1921	John Osborn Polak, Brooklyn, N.Y.
St. Louis	1922	Sidney A. Challanat, Pittsburgh
San Francisco	1923	Harry S. Crossen, St. Louis
Chicago	1924	Frank W. Lynch, San Francisco
Atlantic City, N. J.	1925	Rudolph W. Holmes, Chicago
Dallas, Texas	1926	George Gray Ward, New York
Washington, D. C.	1927	Arthur H. Curtis, Chicago
Minneapolis	1928	Jennings C. Litzenberg, Minneapolis
Portland, Ore.	1929	Carl Henry Davis, Milwaukee
Detroit	1930	James C. Masson, Rochester, Minn.
Philadelphia	1931	Emil Novak, Baltimore
New Orleans	1932	Fred L. Adair, Chicago
Milwaukee	1933	Barton Cooke Hirst, Philadelphia
Cleveland	1934	Joseph B. DeLee, Chicago
Atlantic City, N. J.	1935	James R. McCord, Atlanta, Ga.
Kansas City, Mo.	1936	Lyle G. McNeile, Los Angeles
Atlantic City, N. J.	1937	Pierce Rucker, Richmond, Va.
San Francisco	1938	E. D. Plass, Iowa City
St. Louis	1939	Harvey B. Matthews, Brooklyn, N. Y.
New York	1940	Ludwig A. Emge, San Francisco
Cleveland	1941	Norman F. Miller, Ann Arbor, Mich.
Atlantic City, N. J.	1942	Walter T. Dannreuther, New York
Chicago	1943	No meeting
Chicago	1944	Louis E. Phaneuf, Boston
Chicago	1945	Meeting of House of Delegates only
San Francisco	1946	Philip F. Williams, Philadelphia
Atlantic City, N. J.	1947	Alice F. Maxwell, San Francisco
Chicago	1948	William F. Mengert, Dallas, Texas
Atlantic City, N. J.	1949	Leroy A. Calkins, Kansas City, Kan.
San Francisco	1950	James Ramsdell Bloss, Huntington, W. Va.
Atlantic City, N. J.	1951	Arthur B. Hunt, Rochester, Minn.
Chicago	1952	Louis H. Douglass, Baltimore
New York	1953	Albert W. Holman, Portland, Ore.
		R. Gordon Douglas, New York
San Francisco	1954	Bernard J. Hanley, Los Angeles
Atlantic City, N. J.	1955	Frederick H. Falls, Chicago
Chicago	1956	Frank R. Lock, Winston-Salem, N. C.
New York	1957	D. Frank Kaltreider, Baltimore

Saving the Life of the Woman." M. A. Pallen submitted a prize essay entitled "Treatment of Certain Uterine Abnormalities."

A year later a paper was read on "Tsa-Tsin, or Rhynchosa Excavata, as an Agent of Value in Amenorrhea and Dysmenorrhea," and it "elicited considerable discussion." Another paper, evidently the only other, "was referred to its author to report on more fully at the next meeting of the Association."

At the first New Orleans A. M. A. convention, the Section on the Practice of Medicine and Obstetrics had only medical subjects. In the Section on Anatomy and Surgery, Schuppert, of that city, presented "Remarks upon Some Points Referring to Success in the Operation of Vesico-vaginal Fistula." He said, ". . . bring a sufficient raw surface of the edges of the fistula in close coaptation, and whatever method of operation may be used is of minor importance. A surgeon without that proper skill will fail, whatever method or material he may employ; otherwise he will be successful, provided there is not a constitutional impediment in the patient or some obnoxious cause inimical to healing by first intention; accidents we meet so frequently in practice that it would seem rather strange to expect an exemption in this operation."

Those physicians assembled in the Capitol city in 1870 heard dissertations on "Intra-uterine Injections and Their Therapeutical Value," "Acute Puerperal Mania Treated by Hydrate of Chloral," and "Physiological Laws of Human Increase."

The initial conclave in San Francisco featured a paper on "Criminal Abortion," one on "The Social Evil," and a lengthy report submitted by the Criminal Abortion Committee which concluded with six excellent resolutions.

At the first meeting in Philadelphia one paper was entitled "Three Ovariotomists." Another was "On the Use of Fever and Surface Thermometers." One member "read a letter on a case of stricture of the vagina in a puerperal woman, and desired the opinion of the Section, which was given by several members."

At the 11th annual session of the Section, D. A. O'Donnell continued as Chairman. One topic for discussion was "the physiological anomalies in the configuration of the bony and soft parts of the pelvis, as a cause of retardation of labor." A paper on "The Granular Cell in Ovarian Fluid" was read. The title Section on Obstetrics and Diseases of Women and Children was to be used after this meeting.

The first Chairman's address was delivered in 1874 by Theophilus Parvin, who was A. M. A. President five years later. He spoke on "Uterine Hemorrhage," stating, ". . . it certainly will be one of the noblest triumphs of our divine art when, by an operation so rational, so simple, so speedy as

transfusion, we can rescue woman just when she has passed through the profound sorrow of parturition, just when she is entering upon the supreme joy of maternity, from otherwise inevitable death." He emphasized prevention.

The next year Chairman Byford spoke on "Treatment of Fibrous Tumors of the Uterus by Ergot." He said:

> Recent writers, with few exceptions, teach the entire inefficiency of any form of treatment for the cure of intramural fibrous tumors of the uterus except by enucleation, and this operation is so dangerous and difficult as not to be thought of except in desperate conditions. . . . I conclude my address with the cautionary observation that ergot in the treatment of fibrous tumors of the uterus is a prompt and very powerful agent which cannot be recklessly used without great danger; and that much careful observation is still necessary to enable us to determine the circumstances under which its administration will be both safe and effective.

Marion Sims was the Independence Centennial Jubilee A. M. A. President. S. C. Busey served as the Section Chairman and related, "The written law of this Association limits this address to the discussion of the 'advances and discoveries of the past year,' in obstetric, gynesic and pediatric medicine. However willing or competent I might be to fill the measure of this requirement, the time allowed me would necessarily preclude a critical examination of all the contributions to this department. Nor would this be desirable, since many of them are mere novelties of little or no value, or hasty promulgations of immatured opinions and illogical conclusions." He then proceeded to give an excellent review of the recent literature and lists some 81 references. Referring to an article on the substitution of electrolysis for ovariotomy he said, "So successful has this method proven in the practice of Dr. Semeleder that I hesitate to accept his statement, and am startled at the thought that the greatest triumph of modern surgery is to be superseded by a process so simple and so painless."

1877 to 1887

Chairman James P. White referred to some of the "advances and discoveries of the past year" in his 1877 address. He spoke highly of and predicted a great future for the American Gynecological Society, founded in September of the preceding year. He stated, "In conclusion, I beg to call the attention of this Association to the great neglect on the part of the schools in clinical teaching in obstetrics, and in the diseases of the generative organs. There is no subject in the whole college curriculum which so imperatively demands bedside observation as the process of parturition."

In 1878 Edward W. Jenks spoke on "The Causes of Sudden Death of Puerperal Women," listing numerous references, including one to "the late Professor Charles D. Meigs," who in 1849 in the *Philadelphia Medical Examiner* directed "attention to the possibility of spontaneous coagulation of the blood in the right side of the heart and pulmonary arteries as a cause of death in the puerperal state." In conclusion he stated that the mortality due to puerperal convulsions during the last 20 years had been reduced from 32 to 14% and said, "This is but one illustration of what has been done by our science and art in the past, but it is a significant prophecy of what we may expect in the future."

Chairman Ernest S. Lewis, in 1879, discussed "Abdominal Palpation," "Antiseptic Management in Labor," "Puerperal Fever," "Laparo-elytrotomy," "Primary Conversion of Occipito Posterior into Occipito Anterior Position," "Post Partum Hemorrhage," and advances and progress in "Gynecic-Surgery," including "Censure and Condemnation of Total Extirpation of the Uterus in Cancer," and quoted the brilliant successes of Freund and Schroeder in surgical treatment of cancer. He included a section on "Uterine Fibroids" in his address.

The 1880 Chairman was absent; consequently, G. M. B. Maughs, of Missouri, served pro tem. The Section dropped "and Children" from its name so that it became known as the Section on Obstetrics and Diseases of Women. Papers given included "Battey's Operation in Epileptoid Affections"; "The Management of the Third Stage of Abortion, with Retention of Placenta and Membranes"; and "A Clinical Contribution to the Subject of Removal of the Uterus, in Whole or in Part, for the Extirpation of Tumors Connected with That Organ."

James R. Chadwick chose as his title "Obstetrics and Gynaecological Literature, 1876-1881." He mentioned that the *American Journal of Obstetrics and Diseases of Women and Children* was first published in 1869. He also listed the titles of other periodicals devoted to obstetrics and gynecology published in America and in eight other countries, with dates founded. One table was labeled "Analysis of the Literature of the Year 1880 by Nationalities."

The next Chairman was H. O. Marcy, A. M. A. President 10 years later, who discussed "Fibroid Tumors of the Uterus." He stated, "The peritoneal cavity is no longer the *terra incognita* of the surgeon, nor its invasion attended with the fears or dangers of even a very recent period." He said the growths should be classified as myomas and discussed the various methods of treating them in his thorough and comprehensive presentation.

1883 was the birth year of THE JOURNAL of the American Medical Association. Chairman J. K. Bartlett's address, "Topics in Gynecological Surgery," included discussion of "Extra Uterine Pregnancy," for which he recommended galvanism over faradism. He also advocated its use in such conditions as "Dysmenorrhea" and "Post Partem Hemorrhage."

The next year Thaddeus A. Reamy said, "The editorial criticisms of new doctrines, discoveries, methods, or operations are generally from the pens of those who, by education and special training, have superior abilities for such work. It is, therefore, deemed appropriate on the present occasion, to refer you for an 'Annual Report on Obstetrics and Diseases of Women' to these more fertile and instructive sources . . . . Craving your indulgence, I beg to offer, in lieu of such an address, 'Notes on Two Hundred and Thirty-One Cases of Operation for Laceration of the Cervix Uteri.'" He included discussion of the possibility of cancer originating in lacerations.

R. S. Sutton, M.D., LL.D., in "A Brief Review or the Growth of McDowell's Operation Done at Danville, Kentucky, in 1809: Its Present Status," emphasized that the solitary exception to the original procedure at the end of almost three-quarters of a century was that the ends of the pedicle ligature were being cut short. He eulogized J. Marion Sims, who died in 1884.

S. C. Gordon spoke on "Hysteria and Its Relation to Diseases of the Uterine Appendages." His advocacy of surgery was strong. Although he stated that it was impossible in a majority of cases to determine by touch diseases of organs that produce symptoms, he said that the specimens removed were usually severely pathologically altered.

After stating, "The past year has given few, if any, remarkable discoveries, either in gynecology or obstetrics," F. M. Johnson proceeded to discuss "Ovariotomy," "Hot Water in Shock," "Cocaine in Gynecology," "Caesarean Section" (on which he looked with favor, especially the Sanger-Leopold operation), and "New Pathology in Labor," in which he stressed the etiological relationship between pregnancy and kidney disease, with theories on eclampsia.

1888 to 1899

Chairman Ely Van De Warker spoke on "How Gynecology Is Taught," at the 1888 meeting. The Society Proceedings of the A. M. A. disclose that amendments were offered by H. N. Moyer, including: "The Section of Surgery shall hereafter be denominated the Section of Surgery and Gynecology. The Section on Obstetrics and Diseases of Women shall be abolished. The Section on Diseases of Children shall hereafter be denominated the Section of Obstetrics and Paediatrics."

Under Domestic Correspondence in THE JOURNAL of the American Medical Association, June 8, 1889, there is an unsigned letter entitled "Shall the Section of Obstetrics and Diseases of Women Be Abolished?" which emphasized "both the study and practice of obstetrics and gynecology must remain so correlated that they can only be successfully cultivated conjointly. To abolish this Section of the Association, now so successfully conducted, would scatter the members into other crowded Sections, and do the cause of science and the Association serious injury." The official report of the next meeting, which was held in Newport, R. I., appears in The JOURNAL, July 20, 1889, revealing that a motion to lay the proposed amendments on the table and indefinitely postpone was carried by a large majority. W. H. Wathen presided at the Section meeting, speaking on "Pathology of Ectopic Pregnancy and Pelvic Hematocele."

Chairman William Warren Potter, who was the first secretary of the American Association of Obstetricians and Gynecologists (1888), spoke on some advances during the previous year and suggested that the By-Laws be amended to create a vice-chairmanship, the Secretary's tenure be longer than a year, and the proceedings be published in a separate volume, including stenographic reporting of discussions. Tarnier's traction forceps were referred to as "ingenious and useful." Potter quoted the mandate of the Apostle, "Prove all things; hold fast that which is good."

C. A. L. Reed, the 53rd A. M. A. President, was the 1891 Chairman. Although the *Transactions of the Section on Obstetrics and Diseases of Women* commenced that year, they do not include an address by him, nor have we found it elsewhere. In his biography by Walter L. Bierring, we find him described as "one of the most interesting and dynamic figures in American medicine." The program included "Relation of Gynaecology to Neurology"; "Rapid Dilatation and Curetting"; "Pathological Anteflexion of the Uterus"; Practical Experience in the Treatment of Accidental Abortion"; "Prevention of Puerperal Eclampsia by the Induction of Premature Labor"; "The Operative Treatment of Extra-uterine Pregnancy at or Near Term, with Report of a Case"; and "Extra-uterine Pregnancy."

E. E. Montgomery presented an address on "Some Mooted Points in Obstetrics and Gynecology" the following year. He advocated Braxton Hicks version in cases of placenta previa, reporting a fetal mortality of 70 to 80% and a maternal mortality of 6 to 7%. In discussing "hysterectomy versus supra vaginal hysterectomy in fibroid growths," he recommended total hysterectomy. He referred to two cases of hysterectomy done through sacral resection "with gratifying results."

John Milton Duff gave no formal title but made general references to the objectives of the meetings. Regarding the work of the previous year, he reported it "not characterized by much that was unique or peculiarly brilliant and original." He advised early and prompt therapy for placenta previa, stating that watchful expectancy is "utter absurdity." For puerperal infection he recommended asepsis with early and vigorous treatment, stating that the death rate (2½%) was declining.

In his oration on suprapubic hysterectomy as viewed from the standpoint of personal observation and clinical research, Chairman Joseph Eastman said:

> The century which in a few years will have rolled on to the eternal past, has placed in the magnificent temple of medicine many pillars of surpassing beauty and grandeur, while its surgical columns have risen high toward Heaven where as gilded towers, they fain would vie with the God-given sunshine in dispelling the chill and gloom of human agony.
>
> Chirurgia's tower, thy lights resplendent blaze
> Dries woman's tears, and lengthens out her days;
> McDowell and Sims of our Columbia's clime
> Began the work moved onward nigh sublime.
> To women, then, these blessings shall be given—
> Queen of the home and home the type of Heaven.

Abdominal surgery is *proud* of her past because it is prophetic of her *future*. Even now in the vital present it shall stand forth unchallenged as the crowning glory of all science and of all art.

F. H. Martin's address was on "Some Mooted Points in Pelvic Surgery." He used galvanism in "desperate" cases but said, ". . . in the present state of pelvic and abdominal surgery, I would not voluntarily administer or recommend Galvanism for fibroid tumors, the subjects of which were under 40 years of age, whose tumors were suitable for operative procedures, and whose general health would show an average chance for favorable surgery." He favored hysterectomy instead of removal of the appendages for fibroids, discussed vaginal ligation of the broad ligament to check uterine hemorrhage and to cause atrophy of uterine tumors, stressed the importance of renal evaluation prior to surgery, and recommended silk and antiseptic absorbable ligatures for intra-abdominal operations. He was the first secretary-general of the American College of Surgeons, being one of its founders in 1913.

Joseph Taber Johnson keynoted his remarks on "Puerperal Infection" by emphasizing prevention, namely, "cleanliness and ventilation." He favored the treatment of Lush of New York, who stated, "The more these cases are let alone and the more simple the treatment the more likely they are to get well." He declared, ". . . when the placenta is praevia the uterus should be emptied," as there is "no wisdom or safety in delay." When the cervix was dilated, Braxton Hicks method was advocated. He advised hysterectomy for control of hemorrhage. He gave his reasons for favoring vaginal hysterectomies as "completeness, drainage, avoidance of shock by less handling of intestines, less peritoneal infection, no abdominal wound, and less liability to hernia." In closing he said, "The present Chairman hopes that his successor may be able to report good developments and improvements in the diagnosis of abdominal and pelvic diseases of women, from the evolution of 'x-rays' about which we have heard so much of late. If its promises are fulfilled we ought to find little difficulty hereafter in our diagnosis of extra uterine pregnancy, pyosalpinx, fibroid, dermoid or ovarian tumors."

Milo B. Ward, who occupied the Chair at the Semi-Centennial meeting, reviewed "some of the work which has been accomplished during the last half-century by way of a more accurate comprehension of the etiology, pathology and treatment of diseases of women by our American profession." He said, "The administration of glandular extracts after the removal of uterine appendages and in conditions demanding nutritive tonics, is attracting much attention and [they] are considered by many who have used them to possess much value."

Joseph Price, who spoke of unjust and great opposition to new ideas and techniques, said, "The young school of gynecologists have unfortunately lost interest or neglected plastic surgery." Wider use of pessaries and rest treatment for displacements were advised. He warned, "Be not deterred by false sentiment or the jealousies of those who would rather keep their patients in their own hands than see them cured by others from doing what we know to be our duty." He condemned the current methods of teaching, saying, "the student should be given that which will enable him, when he goes home, to go to work and do good work."

A. H. Cordier praised the A. M. A. meetings, his predecessors and the work of the past. He stressed need for early diagnosis and referred to use of "streptoserum" and "ointment of silver" in puerperal infections.

1900 to 1910

At the beginning of the 20th century, W. E. B. Davis praised asepsis and stressed the need for the use of rubber gloves. He elaborated on the truthfulness of the quotation: "Obstetrics married surgery and the fruit of their union was bright eyed gynecology." He condemned general surgeons for doing gynecologic and obstetric surgery and praised various specialty organizations and their journals. The place of myomectomies was recognized, but hysterectomy was generally considered to be better. He paid honor to Kelly but did not agree with his treatment of "pus in the kidneys through the ureter." The fact that the New York State Medical Society was not then in affiliation with the Association was bemoaned.

Henry P. Newman briefly traced the history of anesthesia by lumbar puncture and recognized it as an anesthetic method but said that the psychic trauma to women "consciously undergoing major operations upon their own viscera and witnessing details of its occurrence" detracted from its usefulness. He thought it was unreliable in obstetrics. His discussion included "Protozoon of Cancer"; "Removal of Lymphatics," in which he referred to Wertheim; "Ovarian Transplantation"; Vinot's work

on "Tubal Epithelium"; and "Permeability of the Amnion." The following quotations are from his address: "Nothing could be more disastrous to the worth and dignity of this specialty, which has occupied for so long so honorable a place in medicine, than to allow itself to be considered and spoken of as one of the surgical specialties." "We are but just arriving at the threshold of the greatest era in our history, in which the full value of prophylaxis is being recognized, and gynecological knowledge and experience are to be the re-creator and conservator of health in women." "There will always be need for intelligent obstetrics while intelligent gynecology should eliminate itself at last by eliminating those conditions which are the cause of disease in women and its only excuse for being. Nothing but gynecology can eliminate gynecology."

J. H. Carstens spoke on "What of the Future?" He said:

> . . . Most questions in the obstetric part of our Section have virtually been settled and those in gynecology are being rapidly settled. Very soon there will be nothing to write about. . . . We should insist that gymnastics and systematic physical exercise should be taught in every school of the land, from the lower to the highest, and that the curriculum of study should embrace the most systematic course of gymnastics to produce a sound body with a sound mind. We should thoroughly study the effects and the results of erotism on the human body. We should study how we can more thoroughly bring about a more perfect marriage relationship and prevent the frequent mismating as shown in our courts. . . . In fact we must more thoroughly study the exact positions of individuals, every combination of physical and mental condition, and their most fit place and proper vocation in life. We must branch out, we must look ahead, we must be counsellors and the guides of the race in the future.

In discussing "The Trend of Gynecologic Work To-day," A. Palmer Dudley said, ". . . with the advent of Lister the Mephistopheles of surgery vanished from view. Fear no longer haunted the mind of operator or patient, and the peritoneum, the bugbear of former years, seemed to readily acquiesce in the evolution. With this confidence in the restorative powers of human nature came the reckless disregard of the consequences in the future." He stated that in 1887 he began "a series of experimental operations on the uterine appendages, which, strictly speaking, was more radical than a hysterectomy, because it trusted such surgical work on the appendages to the efforts of nature for a cure, while the ultimate results were more conservative to the woman, because by the skill of the surgeon and the aid of nature she had been restored to health, and could still consider herself a woman." Due credit was given to Carl Schroeder (1885) as being the pioneer. He said, "In doing conservative surgery on the tubes and ovaries the first thing to do is to endeavor to put the inside of the uterus into a condition to become healthy. If plastic work on the genital canal is necessary, this must be done also. Then open the abdomen and do what work is indicated in each individual case." He classified ventrofixation as a pernicious procedure differing markedly from suspension, the postoperative care of which he narrated.

L. H. Dunning included in "Remarks on Advances in Gynecology During the Last Year" the statement that treatment must be based on ideas of etiology and pathology; consequently, more work was warranted in those fields. He praised the work of Jenner, Pasteur, Koch, Lister, and Tate in discovering many sources of infection and said, "The moral is, let each man find an unsolved problem within the scope of his attainments, and then set himself deliberately and persistently to the task of its solution." He presented an excellent discourse on senile endometritis, and one of his photomicrographs was in color.

C. L. Bonifield commented that the office of the Secretary should be comparatively permanent and that the latter should be relieved of the necessity of disposing of bound volumes of the transactions and should be remunerated for his expenses. He suggested that the number of papers to be read be limited to 30, with only 15 minutes for each paper, and that the longer papers be read in abstract. He recommended changing the name to Section on Obstetrics, Diseases of Women and Abdominal Surgery, with 10 papers allotted to each branch. In discussing "Important Subjects Which Have Occupied the Attention of Gynecologists and Obstetricians During the Past Year," he included surgical and nonsurgical treatment of displacements of the uterus; surgery for cancer, stating that extensiveness of the operation depends on many factors; toxemia of pregnancy, recommending Veratrum viride; and vaginal cesarean section, advised in suitable cases. He also recommended that more work be done on sterility.

"The Legal Responsibility of the Physician for the Unborn Child" was the title used by C. S. Bacon. All physicians were advised to understand their lawful rights and obligations and to have a definite understanding or contract with patients. The fact that the unborn child must be regarded as another human being was emphasized. Consultations were advocated. He said, "In general it might be affirmed that the indications for destructive operations are becoming contracted and many pathologic states that previously were treated by embryotomy, would not now be accepted as indications."

J. Wesley Bovée directed attention to "The Status of the Fight Against Cancer." He discussed occurrence, classification, etiology, and treatment. Among his conclusions were that women should be educated as to signs and symptoms; there should be special care in classification; x-rays and radium are of little use in early cases, in which surgery is best;

radical surgery affords the best results; animal experimentation is promiseful; the vaginal route is not best for total irradiation; there are reasons to believe the disease can be controlled; and cancer should be regarded as contagious.

Walter B. Dorsett's lengthy address on "Criminal Abortion in Its Broadest Sense" was discussed by many participants. He advocated the obligatory teaching of medical jurisprudence and medical ethics in medical colleges, the enactment of good and sufficient laws and the amendment of insufficient laws now on statute books, and the appointment by the A. M. A. President of a Committee on Criminal Abortion for the purpose of attaining better laws through appointed state committees to work with their respective legislatures.

"Mental Alienation in Women and Abdominopelvic Disease" was W. P. Manton's subject. He said, "I and others have demonstrated that relief from suffering brings about a mental palliation often otherwise unobtainable." He believed that mental disease often stemmed from pelvic disorders but noted that it could occur without underlying physical pathology and that operative repair or restoration of the pelvic picture to normal was not always followed by a cure of the mental picture.

John G. Clark's "The Surgical Consideration of Congenital and Developmental Defects Leading to Obstinate Constipation" was so lengthy that a part was deleted prior to publication in THE JOURNAL. He recommended diagnosis by detailed clinical history and skiagraph. His admonition was that this kind of surgery is not for the novice.

1911 to 1920

1911 brought a change in title to Section on Obstetrics and Gynecology, and H. G. Wetherill spoke on "Retrospection and Introspection: Our Opportunities and Obligations." The closing paragraph was, "The crystallization and concentration of ideas, the simplification of practice, and the determination of what not to do, that we have done before, is progress of the best sort. Though this may not be our banner constructive period, it will be none the less valuable to humanity if we learn to see our mistakes of the past and to avoid them in the future."

The following year, under the chairmanship of C. Jeff Miller, "and Abdominal Surgery" was added to the name of the Section. In his dissertation on "The Present Status of Ligation or Excision of the Pelvic Veins in the Treatment of Septic Thrombophlebitis of Puerperal Origin" he said:

> The task of formulating the indications for the surgical treatment of puerperal infection still affords a source of prolific discussion. It seems impossible to agree on established rules as has been done in suppurative appendicitis, gall-bladder infection, or suppurative otitis media. Some of the confusion has undoubtedly arisen from the fact that we have no reliable clinical or laboratory guide to aid us in determining a reasonable prognosis, from the difficulty of differentiating the complex lesions, and to a certain extent, from the antipathy for serious surgical operations on the lying-in woman. It must be said, however, that our ideas are gradually crystallizing, that conservatism prevails, and that, owing to a better conception of puerperal processes in general, surgical measures adopted with more care and discrimination. During the past ten years the possibility of saving by operation the lives of women suffering from puerperal pyemia has received a great deal of attention. The idea is by no means new, as John Hunter suggested it, and scattered reports of successful ligation of the veins of the extremities can be found in the literature of the middle of the past century. The meager material at our command, reported by numerous operators, who have operated without definite indications and without a definitely established technic is sufficient to show that the procedure is feasible and should be given a fair and unbiased trial in septic thrombophlebitis.

1913 brought the birth of the American College of Surgeons, about the formation of which F. F. Simpson stated, ". . . it marks the beginning of a new era in American surgery. Its essential purpose is to encourage the development of sound surgical judgment to render surgeons more skilful and to make surgery more safe. It is not to be an exclusive, but an inclusive organization. It hopes to number among its fellows every one who does safe, sound and honest work." His lengthy address was on "Right-Sided Hypertension with Occasional Cardiac Dilatation as Postoperative Complications." At that meeting W. Wayne Babcock read a meritorious paper on "Spinal Anesthesia in Gynecology, Obstetrics and Abdominal Surgery."

E. Gustav Zinke's title was "A Few Points of Practical Importance in Obstetrics, Gynecology and Abdominal Surgery." He included discussion of "Intestinal Stasis," "Painless Operations," "Roentgen-Ray Therapy" (stating that although good results were obtained on fibroids, surgery was the treatment of choice), "Curative Effect of Radium," "Percy Treatment of Inoperable Carcinoma Uteri," "The Compromise Operations of Obstetrics," "The Treatment of Placenta Praevia" (advising case individualization); and "The Merits of Surgery in the Management of Puerperal Eclampsia," in which he reprimanded a writer who had recently stated the mortality rates were equal in hysterotomy or medical management. He favored use of such agents as Veratrum veride.

Thomas S. Cullen gave a panoramic view of "The Relation of Obstetrics, Gynecology and Abdominal Surgery to the Public Welfare" as he saw them 25 years prior and compared them to those of 1915. In his conclusions are the following statements: "Obstetrics must be made more attractive so that those entering this branch will not be tempted to leave it for less laborious fields." "Any Surgeon opening an abdomen should be capable of doing everything necessary in that abdomen. In other words gynecology and abdominal surgery logically belong together."

Edward Reynolds' scientific address on "Fertility and Sterility, Histologic Study of Spermatozoa, the Ovaries, and the Uterine and Vaginal Secretions in Their Relation to This Question," was well illustrated with photomicrographs.

Howard W. Longyear's discourse on "The Relations of Gynecology to General Surgery, Past and Present" emphasized that gynecology belonged to general surgery. He said:

> The Twentieth Century is ushering in a period of kaleidoscopic changes, of Aladdin-like transformations in everything pertaining to the activities of man. Science, the arts, business, society, finance, methods of warfare—all are feeling the jolts of the erratic and rapid pace of this great evolutionary present-day thrust. We are living in a new world in which habits and customs, venerated by centuries of usage, are dropped without ceremony and without apparent effort or regret, and the new blithely taken on, all in the name of progress. The horse bids fair soon to become extinct as a domestic animal, perhaps to revert to the wild state of his ancestors and be captured and exhibited by future generations of man as a curiosity, along with the gnu, zebra and giraffe.

Brooke M. Anspach's discussion of "Enterostomy and Enterocolostomy in the Treatment of Acute Intestinal Obstruction Following Pelvic Operations" concerned prevention, causes, stages, source of toxemia, and operative measures. He reported five cases illustrated with diagrams.

Thomas J. Watkins referred to the 70th A. M. A. Convention as the "Victory Meeting." He declared, "Democracy has defeated Autocracy." His subject was "Progress in Obstetrics, Gynecology and Abdominal Surgery." He said, "Study of the ductless glands has elucidated much hitherto obscure symptomatology of gynecologic cases, and has opened up a fertile field for further investigation. Radium has proved to be a remedy of great value. Much has been said relative to the practice of surgery by men with insufficient training. It it not my purpose or intent to offer any excuses for them, but to call attention to the fact that some of the responsibility for poor surgery rests elsewhere, especially with the men accountable to medical institutions of learning."

Reuben Peterson emphasized in his address on "The Future of Obstetrics and Gynecology as a Specialty" that they be combined. He condemned the tendency for gynecology to be linked with general surgery but stated that obstetricians and gynecologists must be able and prepared to cope with general surgical problems when they open the abdomen for pelvic disease. "Actual experience and technical skill in abdominal as contrasted with obstetric and gynecologic surgery should be acquired in departmental hospital clinics by cooperation with the general surgical clinics. . . . In fact, this principle of free interchange of services should not be confined to surgery alone, but should apply to all departments of the hospital, where such an arrangement will make for better training in obstetrics and gynecology."

1921 to 1929

John Osborn Polak discussed "The Defects in Our Obstetric Teaching." He recognized the decrease in many conditions "to an almost irreducible minimum" but stated, "Contrast this with the fact that the number of women who die from childbirth is increasing from year to year and that puerperal septicemia seems to be the only form of wound infection the occurrence of which has remained wholly unaffected in the past decade by the advancement of scientific knowledge." He praised classroom instruction but condemned lack of clinical observation in medical schools. "I feel that it is time that the public be taken into our confidence and taught what can be done by prenatal care and clean obstetrics; for good obstetrics would go far toward removing the horrors of childbirth and the consequent dread of invalidism. More than 61 per cent of all gynecologic surgery is the direct result of poor obstetric practice."

"Some Gynecologic Misdemeanors," a paper by Sidney A. Chalfant, contains the statement, "It is far from my intention to give the impression that my criticisms apply to the profession as a whole. There is no finer class of men, or men more conscientious, devoted, and skilful than the medical profession of America." For correction of evils, he advised more careful selection of medical students, more systematic instruction of students in history of medicine, so that they will have the inspiration derived from achievements of the past and receive inspiration for their own work; sufficient and efficient postgraduate schools for training the ambitious; and education of the public as to the necessity of obtaining competent surgical advice.

In his address "Abdominal Surgery Without Detached Pads and Sponges," Harry S. Crossen said, "A sponge left in the peritoneal cavity following an operation constitutes one of the most deplorable accidents of abdominal surgery." He mentioned the increasing number of lawsuits. His method, by which removal of gauze is automatic, was described by narration and eight figures.

Under the title "The Specialty of Gynecology," Frank W. Lynch reviewed the status quo, prognosticated, and outlined a plan of proper training in the future. He stated that gynecology was first to react to surgical possibilities and related how it developed along surgical lines. In his opinion obstetrics needed "a more conservative companion than general surgery." He emphasized the need of well-developed departments in medical schools in which obstetrics and gynecology are taught as interdigitating parts of one major division under con-

trol of one head. Close correlation between the clinic, ward, laboratory, operating and delivery rooms, and follow-up studies were recommended.

In the *Transactions of the Section* we find that the 1925 meeting was called to order by Vice-chairman H. C. Bailey. Apparently Chairman Rudolph W. Holmes was absent. The program included papers on tuberculosis of the vagina; distribution of the ovarian follicular hormone in human genital tissues; the average sex life of American women and the relation between experiences and genital findings; dilatation of the ureter and kidney pelvis during pregnancy; radium treatment of carcinoma of the cervix uteri: results at the Woman's Hospital, New York, after five years; the surgical treatment of varicose veins of the female pelvis; intracranial hemorrhages in the newborn; pelvimetry of the superior strait by means of the roentgen ray; and the treatment of hyperemesis gravidarum by intravenous injections of glucose and carbohydrate feedings.

George Gray Ward in his presentation, "Our Obstetric and Gynecologic Responsibilities," said, "This specialty comprises the study of the physiology and pathology of the reproductive system of woman, and as such should be considered in toto. There is a great need of propaganda to awaken the profession to the fact that obstetrics, as generally practiced at the present, is woefully below the standard that maternity hospital statistics show." He pointed out that septicemia, toxemia, and hemorrhage are responsible for 58% of deaths and are preventable. Condemning practice of bad obstetrics, he stated, "He who attempts to make nature deviate from her normal physiologic processes must remember that, while he may accomplish his immediate object, it is very apt to be at an exorbitant price. Patience is the better obstetrician, in the majority of cases, than dexterity." He emphasized the need of better teaching and training. A classification of wound healing was given. In conclusion he stated:

> I have said that our present shortcomings in obstetric practice must be due to inadequate teaching or a lack of conscience. . . . As to the second cause of our delinquency, what we need today is an awakening of our surgical conscience. Longyear has reminded us that skilful surgeons may not all be conscientious, and conscientious surgeons may not all be skilful. A full appreciation of this can best be brought to our attention by a proper audit of our results. To awaken our conscience, we must be made to appreciate the existing facts by bringing them out into the spotlight—to this end there is no answer but the word "audit." We must audit the morbidity statistics as well as the mortality statistics of our clinics as systematically and accurately as we do our finances —then only shall we see the light that will stimulate us to live up to our obstetric and gynecologic responsibilities.

Discussing "Indications for Surgical Intervention in Pelvic Lesions of Infectious Origin: Based on Seventeen Years of Laboratory and Clinical Study," Arthur H. Curtis included special features of vaginal discharges, endocervicitis, endometritis, and inflammation of the adnexa. He cautioned about operating for sterility alone and mentioned that for years he had tested tubal patency from within the abdomen with air. Conservative surgery was advised, and it was stated that at the time of operation the decision relative to disposition of the ovary required consideration of etiology of pelvic infection and that even though a hysterectomy was indicated the ovaries of young women should be left in situ unless one was dealing with tuberculous or streptococcic infection. He said that operative intervention should be avoided in patients with acute tubal inflammation.

Jennings C. Litzenberg spoke on "Obstetrics and Gynecology in Public Health Program," stating, "Enough facts and procedures are known to reduce the deaths of women by thousands every year if the profession would only apply the knowledge it already has. Why, in the name of humanity, it does not or will not is an enigma. There are enough lives lost which cannot be saved by anything known to medical science. May no more be added to these by neglect." In tabular form he showed the change in the death rate in the United States (1915-1925) as follows: Total puerperal deaths −2%, puerperal infection −11%, eclampsia +5%, cancer of female generative organs +12%, tuberculosis −40%, early infancy −20.5%, prematurity +10%, and birth injuries +14.8%.

Carl Henry Davis chose the subject "Obstetrics and Gynecology in General Practice." He commented on the development of anesthesia and analgesia in obstetric practice; devoted four paragraphs to the "Early History of the Section"; discussed "Maternal Mortality in the United States," saying, "puerperal sepsis still remains the greatest single cause"; and pointed out that "specialists in obstetrics and gynecology were almost unknown eighty years ago. While today there may be one or more in cities of 50,000 or larger, the care of women and children still remains a very important problem of the general practitioner." The need for more and better teaching of obstetrics was emphasized. He discussed "The Training of the General Practitioner" and summarized the conditions believed essential in the effort to obtain better medical care for women patients as follows:

> Governmental activities should be directed toward a careful survey of the causes of maternal and infant deaths in the United States and an investigation of methods that may be adaptable to various local conditions. Medical students who go into general practice after graduation require more adequate clinical training in obstetrics. More institutions are needed in which physicians who wish to specialize in obstetrics and gynecology may obtain the necessary training. There is a great need for graduate nurses who may qualify as midwives to work in conjunction with the medical pro-

fession in the care of a large group of women who are unable to pay for adequate obstetric service under existing conditions.

1930 to 1939

James C. Masson spoke on "The Trend of Present-day Medical Education," stating that it is toward scientific medicine and specialization, which is not altogether due to the desire on part of physicians but is a natural reaction to demand made by the public. He said:

> It is difficult to see a satisfactory solution of the problem of furnishing adequate medical care for all the people at a cost which they can pay, but in recent years investigations which may lead to a solution have been begun. We can await the outcome of these studies, which are in able hands. Our task, meanwhile, I think, should be to help general practitioners to acquire adequate experience in obstetrics and gynecology, and to provide for admittance to the rank of specialists in obstetrics and gynecology only those who at the same time have a sufficient basis in general medicine and sufficient expertness in one special branch to enable them to render adequate service.

In 1931, the Section's annual volume, *The Transactions of the Section on Obstetrics, Gynecology and Abdominal Surgery,* was discontinued. Speaking on "The Biologic Significance of the Female Reproductive Cycle," Emil Novak stated that gynecology's "early history is a record of brilliant achievement in the development of operative procedure, and a subsequent generation has added comparatively little to this branch of our work. . . . Pathology is still, and always will be, a sine qua non in the proper training of the gynecologist. During recent years the line of advance has again shifted, for certainly at the present time physiology must be recognized as the growing margin of our specialty." He acknowledged the help of the anatomists and physiologists. In his discussion of periodicity in the female sex functions we find: "Periodicity may be said to be the rule of the universe." He recorded "some of the accomplishments and some remaining problems" and concluded with "the female sex cycle as distinguished from the female reproductive cycle." His closing paragraph expressed dependence on our allies in the laboratory, and he quoted from one of his papers: "So long as we recognize this dependence, and so long as we are willing to follow the line of scientific march rather than cavort ahead of it, we may perhaps be pardoned for an occasional display of overenthusiasm. After all, the latter is usually due to the fact that we have human beings to cure, just as the laboratory worker has scientific problems to solve."

Fred L. Adair, first president of the American Committee on Maternal Welfare (1934) and first president of the National Federation of Obstetric-Gynecologic Societies (1945), spoke on "The Interrelationship of Mother and Fetus" at the 1932 meeting. Included in his statements were these: "The exact relative importance of heredity and environment is not known." "We know that certain toxins will destroy germ cells. In all probability, they are subject to injurious influences which may not destroy their potency but which lead to subtle changes." He discussed "The Critical Early Period of Pregnancy," "Hormones," "Pathologic Conditions," and "Other Changes." His concluding sentence was, "These relationships are affected by the heredity of the parents, by the growth and development of the potential mother, by the character of the germ cells, by the maternal environment throughout pregnancy, by the critical period of parturition and, to a lesser degree, during the postpartum and postnatal periods."

Barton Cooke Hirst discussed "The Four Major Problems in Gynecology." He thought that "one of every eight women who reach the age of 35 will have cancer" and stated that there should be provision for both surgical and radium treatment. Concerning maternal mortality he said, ". . . half of these deaths are preventable." He considered "sterility" and "birth control." His address was somewhat philosophical and was terminated as follows: "In attempting to review so much in so short a time, I am aware that I give only the merest hints that may, perhaps, invite others to more productive thought, especially the younger members of the profession. We may confidently leave to them the problems vexing us. It is certain they will reach for higher levels of achievement than we have attained."

Joseph B. DeLee in his "Obstetrics Versus Midwifery" stated that contrary to the dictionaries he did not consider these terms synonymous; "midwifery is the practice of midwives, male or female, and obstetrics is the practice of the scientifically trained physician." He traced the historical development of midwifery and pointed out:

> . . . Until very recently the practice of normal obstetrics by physicians has been looked down on by the profession and by the public as well as by the midwives. . . . The public in many places still believes that his [the obstetrician's] accomplishments are less than those of the medical men and the surgeon. The medical schools, in many universities, still rate obstetrics as a minor specialty. . . . Hospitals do not provide equal facilities for obstetrics as for surgery. . . . All my medical life I have striven to eradicate this low opinion of obstetrics and to place on equally high pedestals the three primary branches of medicine, obstetrics, medicine and surgery, all equally important, all equally dignified.

He discussed "Disturbances of Pregnancy," "Labor," "A Natural Delivery," and "Attainment Through Education," bemoaning the fact that there were insufficient schools, teachers, material, and support. He believed in teaching the beauties of normal obstetrics, asepsis, intelligent expectancy, and trusting in nature.

James R. McCord, who was to be the first president of the South Atlantic Association of Obstetricians and Gynecologists three years later, was the 1935 Chairman. His presentation on "Syphilis and Pregnancy: A Clinical Study of 2,150 Cases," contained many statistical studies. His conclusions were as follows:

1. Pregnancy does not affect the reliability of the Wassermann reaction. 2. This test should be a routine part of antepartum care. 3. Regardless of the activity of the disease, sufficient antepartum antisyphilitic treatment assures the woman a syphilis-free baby in 95 per cent of the cases. 4. The best results will be obtained with ten or more treatments. 5. Treatment should be mild but continuous and should not be controlled by the Wassermann reaction. 6. The concurrent use of arsenic and a heavy metal has worked well in our hands. 7. Such therapy seems to be safe for the mother. 8. In the vast majority of cases, a strongly positive cord Wassermann test, properly done, means that the baby has congenital syphilis. A negative cord Wassermann reaction is of little value in the diagnosis of congenital syphilis. 9. The characteristic picture of osteochondritis of the long bones is pathognomonic of congenital syphilis. 10. There seems to be no condition in medicine that returns such huge dividends in life and health with such a small output of energy and money as that seen in the prevention of congenital syphilis.

In "Trends in American Obstetrics During the First Third of the Century," by Lyle G. McNeile, we find the opening sentence: "Although many notable advances and changes have been made in the practice of general medicine and surgery during the present century, in no specialty have there been more drastic changes than in obstetrics." He pointed out: ". . . at the beginning of this century every general practitioner had perforce to be an obstetrician; but at this time the new fledged doctor obtained his diploma to practice with little or no actual experience in clinical obstetrics. There were at this time not more than a half dozen medical schools that maintained lying-in hospitals in which medical students could witness deliveries, and the student who had actually delivered one or two women before he was graduated was considered very lucky." He discussed "The Dawn of New Obstetrics," "Causes That Contributed to the Changed Tendencies in Obstetrics," "Trends of the New Obstetrics," "Obstetric Education," "Is Pregnancy a Disease of Nine Months' Duration?," "Trend Toward Making Obstetrics Easier for Patient and Physician," "The Elimination of the Midwife," and "Apparent Trends Characterizing Obstetrics in Present Century."

Pierce Rucker discussed "The Treatment of Eclampsia," dividing it into two parts: preventive and curative. He strongly emphasized the former, stating that it should start when there is a rise in blood pressure or unusual gain in weight. Statistics on 129 treated cases were related under the headings "stopping the convulsions," "good nursing care," "promoting kidney function," and "digitalis," of which adequate dosage was deemed mandatory.

The Section on Obstetrics and Gynecology was the title used beginning in 1938. In "The Undergraduate Teaching of Obstetrics," E. D. Plass discussed factors relating to the problem and offered "a considerable defense of the men now actually engaged in obstetric teaching." It was pointed out that modern obstetrics is actually a field of preventive medicine. Didactic obstetric teaching was rated par with instruction in the other medical clinical branches, but it was emphasized that the clinical instruction could not be expected to result in competency to handle all obstetric emergencies. He pled for the more effective utilization of the trained and experienced obstetric specialists but appreciated the fact that changes in medical thought would inevitably be involved, requiring time.

Harvey B. Matthews directed attention to "Obstetric Shock: Its Causes, Recognition and Management." An historical account is given. The primary principles were elaborated. His concluding statement was as follows: "Real progress in the prevention, recognition and management of shock lies not only in cultivating the art of obstetrics but in the study of biologic principles that concern reproduction, function, nutrition, metabolism and the repair of tissues, and in the thoughtful application of this knowledge. With the mastery of these principles clinical experience and the maturity of years will give that degree of sound judgment which every physician doing obstetrics—general practitioner or specialist—longs to attain."

1940 to 1949

The 1940 address of Ludwig A. Emge, "Present Trends of Socialization of Medicine in Relation to Maternal Welfare," exemplifies intelligence and foresight, as time has proved. In a discussion of the aim of socialization, the national health program, the care of migratory workers in California, hospitalization, and the position of physicians in administration, the plea is made for enlightenment of the profession, the development of sound convictions, and "action—organization and cooperation —and this must come from within our ranks."

The following year Norman F. Miller discussed "The Perpetuation of Error in Obstetrics and Gynecology," listing the circumstances which "combine to make our time particularly susceptible in this respect" as the World War; "endocrinology, the beautiful romantic young maiden of modern medicine, who keeps us dizzy with her therapeutically provocative gyrations;" overzealousness in the field of medical writing; and blind adherence to obsolete ideas in our specialty. Careful consideration was given to "Errors That Are Being Perpetuated," "Perpetuation of Obsolete Standards," and "What to Do About It." He closed with this sentence: "If

we recognize our responsibility and accept this challenge, if we are unafraid and willing to think and plan in terms of a newer and better standard of medical care for the pregnant woman, then I foresee for obstetrics, for maternal and child health, a new and great future."

The 1942 address, "The Educational Objectives of the American Board of Obstetrics and Gynecology," presented by Walter T. Dannreuther, president of the board since its founding 12 years prior, deserves to be read in its entirety.

The 1943 meeting was scheduled for San Francisco, but, because of war, only the Board of Trustees, Executive Committee, and the House of Delegates met. The next year, Louis E. Phaneuf's "The Changes in Operative Gynecology During the Last Quarter-Century" was summarized as follows:

> The last quarter of a century has shown significant improvement in surgical technic, with emphasis on careful dissection and ligation of individual vessels with fine material rather than mass ligature of tissues. The treatment of carcinoma of the cervix has changed from surgery to irradiation with the return to the radical pelvic operation by a few gynecologists in early cases and good surgical risks. Carcinoma of the uterine corpus and fundus has remained a surgical lesion, surgery, however, having been complemented by irradiation. Improvement in the operation of myomectomy has resulted in more conservative management of these lesions in the young; supravaginal hysterectomy still remains the common method in use, while an increasing number of gynecologists have turned to panhysterectomy as a prophylactic means against carcinoma of the cervical stump. Vaginal hysterectomy has been reborn and improved and has now become a commonplace procedure. The increased number of surgical vesicovaginal fistulas has been responsible for the elaboration of new technics in the cure of this lesion.
>
> Trachelorrhaphy and amputation of the cervix are less frequently done, these having been replaced in many cases by cauterization and electrocoagulation. A significant advance has been made in the surgical treatment of uterine prolapse, cystocele, and rectocele through better anatomic understanding of these lesions and by reconstructing the deficient supports through the vagina rather than by depending on abdominal suspension or fixation of the uterus. Pelvic inflammatory disease has been handled more and more by conservative methods, and the sulfonamide drugs seem to show great promise in lessening and eradicating this condition. Ovarian tumors have been better classified, the rare tumors have been discovered, the tendency of malignant changes in these neoplasms has been emphasized and their early ablation has been strongly advised.

The 1945 meeting was canceled due to war, and only the Board of Trustees, Executive Committee, and House of Delegates met. The next year, Philip F. Williams, to whom should go the highest of praise for his efforts in bringing into existence in 1951 the "national organization for ethical, competent obstetricians and gynecologists," spoke on "Maternal Welfare and the Negro." The reprint distribution of this address was considerable. His closing paragraph was as follows: "Obstetric care has undergone an evolution in this generation, but the Negro has not participated fully in the benefits of modern obstetrics. It is not possible to have two systems of maternal welfare; there must be one all-inclusive health program. Health education and adequate maternity care for the Negro are amply provided for in the proposed national health program of the American Medical Association. Conservation of human life in the process of reproduction should be shared equally by all Americans. The interest and activity of the medical profession can bring this about."

Alice F. Maxwell was in the Chair at the A. M. A. Centennial session of the Section. Her subject was "A Medical Inventory." Unfortunately, this address evidently was not published and a copy of the manuscript is not available.

William F. Mengert's "Estimation of Pelvic Capacity" included the listing of the five components of cephalopelvic disproportion as "size and shape of bony pelvis, size of fetal head, force exerted by the uterus, moldability of the head, and presentation and position." His discussion of subjects, methods, interpretation, and results and his comments are excellent and should be read in full.

1950 to 1957

"Reproduction in the Older Woman" was the title of the address by L. A. Calkins, and it included 10 tables of interesting data. In his summary and conclusions he stated:

> Older pregnant women, like other women of the same age but not pregnant, are more apt to have fibroids, hypertensive cardiovascular disease and, perhaps, carcinoma than are younger women. They are, therefore, deserving of the most careful and complete examination of all their organs and functions. The analysis also seemed to show that labor and the results thereof, except for a possible extremely moderate increase in fetal mortality, can be expected to progress along the same lines as for the younger groups. Our present fear of the outcome of pregnancy for the elderly primigravida is no more justified than would be such a fear for the elderly multigravida.

James Ramsdell Bloss, Chairman of the A. M. A. Board of Trustees in 1944, discussed "Causes of Fear Among Obstetric Patients" in his 1950 address, emphasizing that obstetricians and gynecologists must understand and "practice the humanities as well as the science of the medical profession." He included discussion of "Fears with Psychologic Basis," "Basic Conflicts," and "Fears with Legitimate Basis." It was pointed out that there has been too much disturbing publicity about the Rh factor. Frank, encouraging discussions with patients in the light of scientific medical accomplishments were recommended.

"The Test of Labor—An Evaluation of Its Present Worth," by Arthur B. Hunt, contained 10 tables. His conclusions were well drawn. They included this statement: ". . . to date there is no better way to justify an initial cesarean section than a failed test of labor." It also tests the obstetrician's "powers of observation, vigilance, judgment, obstetric conscience, and technical skill."

Louis H. Douglass spoke on "Repair of Obstetric Soft Tissue Damage Immediately Post Partum," based on an experience of about 17 years of practice, under the headings of "Cervical Repair at Delivery," "Perineorrhaphy at Delivery," and "Advantages of Elective Perineorrhaphy." He had been pleased with his anatomic results, and the expressions of gratitude from patients had been very rewarding.

Albert W. Holman was elected to the chairmanship for the 1953 meeting, but he died in 1952, being succeeded by Vice-chairman R. Gordon Douglas.

"The Challenge of Dystocia" was the subject of Chairman Bernard J. Hanley. His second paragraph began, "Prolonged labor per se is not necessarily harmful, but prolonged labor accompanied by a difficult forceps operation is a combination that always causes injury to the mother and is frequently lethal to the baby." He emphasized that patients in prolonged labor should be properly sedated and given adequate fluids. He and his co-workers had obtained excellent results in determination of the anterior pelvic depth by the use of the Hanley-McDermott pelvimeter, which he considered a rational procedure for determining the possibility of midpelvic or outlet dystocia.

Frederick H. Falls spoke on "Conquest of Eclampsia." A résumé of this is as follows:

The convulsive stage of eclamptogenic toxemia has been gradually eliminated in three hospitals over a period of 20 years, despite the fact that eclampsia remains one of the three most common causes of maternal mortality in the country as a whole. The improvement is related to the increasing frequency with which toxemia is recognized and the systematic attention given to it. The mild nonconvulsive forms of toxemia, found and treated early, are without much danger. It is the convulsive stage of the disease that does irreversible or fatal damage. A simple program of management that has been developed must be brought to bear as soon as toxic symptoms appear and must be continued until the symptoms are brought under control or the patient is delivered. The program includes strict prenatal care, hospitalization if ambulatory care proves insufficient, induction of labor if the toxemia progresses, and cesarean section if certain indications exist. Although more knowledge of this disease is needed, the means for preventing most of the deaths that now occur are already available.

In 1956 Frank R. Lock discussed "A Concept of Operative Gynecology," which he summarized as follows:

Operative gynecology is a major field of medical practice. Although the pathological significance and natural history of pelvic lesions is well known, the methods of management by the profession at large are variable. The arbitrary application of surgical procedures, according to the basic principles of the removal of pathology or correction of anatomical defects, is not acceptable in the field of gynecology. The effects of a given operative procedure must be weighed against the consequences of other management of existing pelvic pathology. It is possible to establish beyond a reasonable doubt that relief of symptoms will result from operative or nonoperative treatment in gynecology, through exact diagnosis and appraisal of the related pathologic, physiologic, and psychologic processes of women.

In 1957 D. Frank Kaltreider gave an address on "Fetopelvic Grading of Breech Presentations." THE JOURNAL's summary follows:

In the management of a breech presentation, three factors must be considered in order to decide between vaginal delivery and cesarean section. These are (1) pelvic size, (2) pelvic shape, and (3) estimated fetal weight. Pelvic size can be accurately measured by x-ray pelvimetry. Unless the infant is premature, vaginal delivery is contraindicated in flat pelves with an obstetric conjugate of less than 10 cm. Fetal weight is best estimated by having four or more examiners give an estimate without the knowledge of others and averaging the estimates. In addition to the above three factors, the behavior of the sacrum and consideration of uterine inertia must also be taken into account.

Comment

Conceived by its 12-year-old mother, the A. M. A., the Section was born at term in 1860, being given the name "The Section on Practical Medicine and Obstetrics." That appellation was subsequently changed as follows: 1867, Section on Practice of Medicine and Obstetrics; 1873, Section on Obstetrics and Diseases of Women and Children; 1880, Section on Obstetrics and Diseases of Women; 1911, Section on Obstetrics and Gynecology; 1912, Section on Obstetrics, Gynecology and Abdominal Surgery; and 1938, Section on Obstetrics and Gynecology. Prior to 1958, the Section had held 93 meetings in a total of 30 cities, including Atlantic City, N. J., Chicago, and San Francisco, ranking in that order of frequency. War caused cancellation of the 1861, 1862, 1863, 1943, and 1945 meetings. The life of the Section has at times been impassioned and troubled, as exemplified by the Civil War years and the proposal of an abolition amendment in 1888. It has had its hours of bitterness and its reports of tragedy, but these are greatly outweighed by its superb and glorious hours. Mindful of its accomplishments and thankful to the Great Physician for them, we look to the future with anticipation of continued progress and happiness.

4240 Magnolia St. at General Pershing (15).

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ANTICOAGULANTS—A COOPERATIVE EFFORT

THE advent of heparin and bishydroxycoumarin (Dicumarol) in the late 1930's and early 1940's as useful drugs for the management of thromboembolic disorders started a chain of events that went far beyond their use as agents for the treatment of thrombophlebitis. Anticoagulants have become generally accepted in the management of long-term and short-term therapy of coronary artery disease and myocardial infarction [1] and for the prevention or amelioration of certain cerebrovascular diseases.[2] Their availability has opened new areas of investigation into the mechanism of blood coagulation. Their promising use in cerebrovascular disease has occasioned a new and more precise classification of cerebrovascular diseases because, in the words of a committee of the Advisory Council for the National Institute of Neurological Diseases and Blindness, Public Health Service, the practitioner now has available powerful drugs which alter the coagulability of the blood. Hence diagnosis now becomes imperative not only as a means of directing therapy but also for further scientific study.[3] A premium is now placed on diagnosis of cerebrovascular disease, for the days of fruitless therapeutic maneuvers may be past.

Public interest in these drugs is reflected by the news concerning the President's use of an anticoagulant and more recently by the direction of the Senate Appropriations Committee to the National Institute of Health to study the action and utilization of anticoagulant drugs as aids in the treatment of coronary and cardiovascular disease (strokes). The directive was backed by a 2-million-dollar appropriation (Senate Report No. 17191, 85th Congress, 2nd Session, p. 28).

No less important has been the development of new coumarin compounds that made the use of anticoagulants more practical than bishydroxycoumarin, the first of the synthetic anticoagulants. Unfortunately, no useful substitute for natural heparin has appeared. Several recent reports in THE JOURNAL on warfarin sodium are examples of progress in that direction.[4] Interestingly enough both drugs had their origin in the same laboratory at the University of Wisconsin. Of equal interest is the fact that these valuable additions to the drug armamentarium came from unfettered research or as Link, the discoverer of bishydroxycoumarin and of warfarin, put it: "I think the secret of their success (his students) is three-pronged: they never ceased to wonder; they kept on trying, and they were on a project toward doing mankind some good instead of trying to destroy it." In these words, the aim of American medical research can be summed up.

Useful modalities in science and medicine do not come in full bloom. They develop by slow stages and from devoted workers. A review of the progress of the past 20 years in a symposium honoring the late Dr. Jay McLean by those intimately involved has recently appeared.[5]

Dr. Irving S. Wright, one of the most active proponents of anticoagulant therapy, pointed up the diseases susceptible to control by anticoagulants: "Today, throughout the civilized world and on both sides of the iron curtain,[6] anticoagulating drugs are used in a steadily increasing number of conditions. They are under study in hundreds of institutions. It is estimated that over one million persons suffer from thrombosis or embolism in the United States each year. These conditions include idiopathic, postoperative and traumatic thrombophlebitis, myocardial infarction, rheumatic heart disease with embolization, thromboembolism in pregnancy, peripheral arterial thrombosis and certain selected examples of cerebral thrombosis and embolism. More than four hundred thousand persons die each year with thrombosis or embolism as the terminal event. For each of these conditions and for many others, anticoagulant therapy has been used and should be considered. For some the indications are well established, for others the final chapters have not been written."

The four speakers, Drs. Irving S. Wright of the New York Hospital, Charles H. Best of Toronto, Canada, Armand T. Quick of Marquette University, Milwaukee, and Karl Paul Link, each presented his part in this story, which has since captured the interest of legislators.

Thanks to Dr. Wright, the reader can see the part played by the Association through its then Council on Pharmacy and Chemistry in the early

days of bishydroxycoumarin. Several of his early patients developed hemorrhagic complications which had not been noted by those who worked with the compound earlier. He reported this incident and thus prevented the premature release of the drug until fully adequate studies permitted the development of safe directions for use. Through the action of the Council, many tragedies were averted by this cautious step. Indeed, this step may have averted the possible rejection of the coumarin anticoagulants in these early trying days. The reasons need not be detailed further than to point out that adequate methods for clinically controlling the reversible hypoprothrombinemia had not been fully developed. Fortunately, time and experience have placed the control of the reversible hypoprothrombinemia in proper perspective and on sound ground.

The method most commonly used to regulate dosage of bishydroxycoumarin and other anticoagulants which stemmed from it is the one-stage method, developed by Dr. Armand J. Quick. The test is taken for granted today, but the recital of the steps to reach this goal were retraced by its discoverer. Without the test or its modifications the availability of clinically useful anticoagulants would have been delayed. The use of a prothrombin determination cannot, as yet, be divorced from the administration of anticoagulants. Both complement each other. Just as the drugs themselves led to newer understanding of blood coagulation and the use of drugs which alter it, the newer methods such as prothrombin consumption time, the partial prothrombin test, and the thromboplastin generation tests are outgrowths of the one-stage prothrombin time test.

While the coumarin compounds are commonly associated with the term anticoagulant, the fact that the isolation of heparin and its use in thrombophlebitis antedated bishydroxycoumarin as an anticoagulant drug is often overlooked.

Modern heparin is due largely to the efforts of the late Dr. Jay McLean, who became interested in it as a student at Johns Hopkins University. In the very personal account of McLean's involvement with heparin, Dr. Charles H. Best of Toronto traced an item of purely physiological interest to therapeutics. This effort was truly international, for with the availability of purified heparin, Dr. Gordon Murray of Toronto made clinical trials in 1935, followed by Drs. Eric Jorpes and C. Craaford of Stockholm. The early finding that certain types of clinical thrombosis could be prevented by treatment with heparin has been amply confirmed.

It was early recognized that heparin, while an effective agent for prevention of clinical thrombosis, had serious disadvantages. The supply was limited by virtue of a limited supply of starting material, lung tissue; because it was active only on intravenous use, its action was short and consequently highly expensive.

The meeting of purely physiological and clinical studies came about originally through a veterinary and agricultural problem. Link, of Wisconsin, in 1933 started out to develop a strain of sweet clover which would not impart the hemorrhagic disease noted earlier in cattle who were fed on silage made from sweet clover. How the goal turned from cattle to man was told by Link. But bishydroxycoumarin was only the beginning of a large number of synthetic derivatives related to the parent compound, for as Link, the chemist, forecast in 1944, "we might be at the beginning of things and not at the end in this field of study." [7] The clinician, E. V. Allen, who was among the first to use bishydroxycoumarin clinically echoed in 1946 a similar sentiment: "Advantageous as both heparin and Dicumarol are, use of them represents only the first steps in the direction of securing satisfactory anticoagulants for clinical use." [8]

In the years intervening between the isolation and synthesis of bishydroxycoumarin, Dr. Link and his students set themselves another goal—to obtain an anticoagulant compound which would have "most of the desirable features that can be expected from an anticoagulant that can be given via the oral route." Earlier the clinicians virtually snatched a "cow-poison" for a human drug, but accepting a compound with a high rodenticidal value as a human drug was not so readily done. Fortunately, an aborted suicide attempt with a rodenticide containing warfarin paved the way. An article in THE JOURNAL" detailed the recovery of a patient after ingestion of large amounts of warfarin. In due time, the Wisconsin group provided water-soluble warfarin sodium for clinical use. The appearance of a score of papers on this compound since its introduction in 1954 led Link, the last of the quartet, to state: "It is my firm belief that in time it [warfarin sodium] will replace Dicumarol on the basis of its performance over a wide variety of conditions and that other anticoagulants of the Dicumarol type [including the many made in the Wisconsin laboratories] will not be superior." This view by one who has been responsible for the original impetus in this field represents a standard for future anticoagulant compounds. Whatever the future may bring in this respect, the physician who uses anticoagulants will want to keep in mind the triad of Link for successful use of anticoagulants. Successful anticoagulant management calls for (1) clinical judgment, (2) proper prothrombin determinations, and (3) the ready availability of vitamin K. The current literature on anticoagulants indicates that this is being heeded.

Thus the clock has made a full turn. The isolation of heparin by McLean and its purification by the Toronto group, the turn of a hemorrhagic dis-

ease of cattle to a human drug, the development of new methods to study blood coagulation processes, the establishment of the value of anticoagulants in the treatment of myocardial infarction and a host of other thromboembolic conditions, the initiation of studies to assess their value in prevention and amelioration of strokes, and a new classification of cerebrovascular disease occasioned by these findings represent an excellent example of synthesis of laboratory and clinical developments going hand in hand.

Here is a historical account of unfettered research by free men at their best who set out to do some good instead of trying to destroy life. Here is a story of the intertwining of isolated effort; all the strands of which are playing a significant role in the present and future control of atherosclerotic and thromboembolic disease. Clinicians and laymen alike will watch with interest a forecast recently made: "If these trends are corroborated [reduction of morbidity in coronary artery disease], long term anticoagulation is the first distinct preventive agent in arteriosclerotic disease." [10]

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INCOME TAX GUIDE

Last year, on March 1, 1958, THE JOURNAL published a special edition entitled "1958 Federal Income Tax Guide for Physicians." Copies of this guide are still available on request to the A. M. A. Law Department, 535 N. Dearborn St., Chicago 10.

LONG DISTANCE TELEMETERING AND MONITORING

The development of lightweight radio equipment for artificial satellites to transmit back to the earth environmental information about space and planets may also assist physicians and physiologists to gather physiological data on human beings and animals while ambulant and with normal freedom of movement. The equipment need not be so rugged as to withstand the large accelerative forces of a rocket but can be sufficiently sturdy to resist damage of accidental falls and to function under the vigorous bodily movement of athletes and men and women at their regular work. The equipment could record data also on sedentary patients.

Miniature broadcasting equipment and its uses have been dealt with in an article by Beenken and Dunn.[1] They visualize transmitters of not more than 2 lb. (0.9 kg.) in weight that can be operated by persons without radio engineering experience and that are nondirectional, within the tolerance of Federal Communications Commission recommendations, and with battery life of at least 100 hours.

Beenken and Dunn mention a list of physiological functions that can be studied with reasonable accuracy, such as temperature, pulse pressure, exercising tests, and oxygen demand. The physician might study cardiac output potential and record electrocardiograms while his patients are working at their regular jobs, and he might observe physical and physiological effects on patient-executives at the conference table. In the event the transmitter is made smaller (and one has already been made small enough for a man to swallow), the physiological changes in athletes may be observed while they are participating in competitive sports. Undoubtedly much discussion will ensue if and when football coaches read meters of electronic instruments to determine whether a player is tired and at the point of exhaustion.

These are a few of the achievements to be realized in the near future by the cooperative efforts of physicians, physiologists, and engineers. Increased interest in medical electronics is exemplified further by such meetings as the Conference on Electrical Techniques in Medicine and Biology, held in Minneapolis after the recent A. M. A. Clinical Session, and the meeting in New York, March 23-26, of the Institute of Radio Engineers, which has scheduled papers dealing with the applications of electronic tools and instruments to physiological, diagnostic, and clinical procedures.

1. Beenken, H. C., and Dunn, F. L.: Short Distance Telemetering Physiological Information, IRE Transactions on Medical Electronics, December, 1958.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Nine months ago the Chairman of the A. M. A. Board of Trustees, Dr. Leonard Larson, pledged our Association to a dedicated and continuing effort to improve the health care of the aged. He made this vow in testimony before members of the House Ways and Means Committee in Washington, D. C.

Has the A. M. A. kept Doctor Larson's promise? Has medicine taken specific action at the national and state levels on the aged problem?

The answer is an emphatic yes. For example, the A. M. A. House of Delegates took farsighted action when it approved a proposal calling for development of an effective voluntary health insurance or prepayment program for the group of persons over 65 years of age with modest resources or low family income. Within three months official groups of several states—West Virginia, New Jersey, California, Texas, Ohio, Michigan, Florida, Iowa, and others—moved decisively on the A. M. A. policy recommendation. In addition, 34 state medical societies will give the matter top priority at their annual meetings this spring.

What are some of the states actually doing? In West Virginia the Association's Committee on Blue Shield has recommended that physicians accept 50% of their normal fees for Blue Shield clients over 65 years of age who have an income not exceeding $3,000 per annum. New Jersey has approved the A. M. A. policy and urged the Medical-Surgical Plan of New Jersey (Blue Shield) "to prepare a contract offering coverage at reduced premiums to people over 65 with reduced income."

Your A. M. A. also is working closely with commercial insurance organizations to encourage the development of new insurance programs and expansion of existing lower-cost protection.

Policies already available include some guaranteed renewable contracts, "paid-up-at-65" policies, senior security contracts, and "65-plus" policies. To further strengthen and improve private insurance coverage for those over 65 years of age, the Health Insurance Association of America has asked its 265 member companies to make available (1) policies guaranteed renewable for life, (2) coverage to persons now over 65 years of age, (3) coverages that will continue after retirement, and (4) the inclusion in the group contract of the right to convert to an individual contract at end of employment.

Through medical societies and the insurance industry sound and inexpensive protection to persons in the senior citizen bracket is being broadened and improved faster than many thought possible only a few months ago. We are not, however, confining our efforts to the development of financing mechanisms only. Solution of financial problems relating to the health care of the aged also depends on reductions in the costs of services.

Your A.M.A. believes that there is an undeniable need for new and improved facilities tailored to the specific health requirements of older citizens. Therefore, we vigorously support a government-insured loan program of the FHA type for nongovernmental hospitals and nursing homes whether their ownership is of a nonprofit or proprietary nature. We also recommend changes in the Hill-Burton act to make it possible for states to put more money into nonprofit nursing homes.

These then are some of the forward steps taken by your Association, the state medical societies, and the health insurance industry to improve the health care of the aged. No one can deny that there has been solid progress; we cannot deny that there is still much to be done. However, medicine and the members of the health team are in positive, forward motion against problems that not long ago may have seemed insurmountable.

GUNNAR GUNDERSEN, M.D.
La Crosse, Wis.

MEDICAL NEWS

ALASKA

Annual Meeting Held in Juneau.—The Alaska State Medical Association held its 14th annual meeting March 19-21 in Juneau under the presidency of Dr. William M. Whitehead. The guest speakers were Drs. Edward Morgan, clinical assistant professor of medicine, University of Washington Medical School, Seattle; Raymond F. Peterson, division of pathology, Murray Clinic, Butte, Mont.; and Robert A. Pommerening, clinical assistant professor of dermatology, University of Washington Medical School, Seattle. Addresses were given by Acting Governor Hugh J. Wade and Mr. M. L. MacSpadden, Mayor of Juneau. A panel discussion on "Ulcerative Colitis and Irritable Bowel Syndrome," held March 20, was moderated by Dr. Morgan. A film, "Surgical Repairs of Facial Lacerations for Optimum Cosmetic Results," and exhibits were held. The banquet, the evening of March 20, was held at the Baranof Hotel. A ladies' program was also arranged.

CALIFORNIA

Radiologist Given Award.—The Gold Medal of the American College of Radiology has been awarded to Dr. Robert S. Stone, chairman, department of radiology, University of California School of Medicine, San Francisco. The Gold Medal is presented annually "for distinguished contributions to radiological medicine." Dr. Stone joined the university faculty in 1928 and became professor of radiology in 1938. From 1942 to 1946 he was associate project director for health at the Chicago Metallurgical Laboratory of the atomic bomb project. After the war he developed and now directs the Radiological Laboratory at U. C. Medical Center, where physical, chemical, biological, and clinical investigations are conducted with the 70-million-volt synchrotron.

Name Dr. Kretchmer Department Head.—Dr. Norman Kretchmer, associate professor of pediatrics at Cornell University Medical College, New York City, and associate attending physician at New York Hospital, will succeed Dr. Robert H. Alway as head of Stanford University's pediatrics department, effective July 1. Dr. Ruth T. Gross, associate professor, has been acting head of pediatrics for the past two years. Dr. Kretchmer spoke in San Francisco Feb. 24 before the Northern California Chapter of the American Academy of Pediatrics. Last year the academy presented him with the E. Meade Johnson award for distinguished pediatric research. Dr. Kretchmer has taught at the University of Minnesota, Minneapolis, and the State University of New York.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

COLORADO

Biography of Florence Sabin to Aid Research.—The University of Colorado Press, in connection with the state's Rush to the Rockies centennial observance, is publishing "Florence Sabin: Colorado Woman of the Century," a 222-page book, written by Mrs. Elinor Bluemel, of Englewood. The book traces the life of Dr. Florence R. Sabin, world-famous medical researcher, teacher, and humanitarian, who died in 1953. It contains eight pages of photographs. All royalties from the sale of the book will go to the University of Colorado School of Medicine for research in cellular biology. A statue of Dr. Sabin was dedicated Feb. 26 in Statuary Hall in Washington, D. C. She is the first Coloradan to receive such an honor. Born in Central City, Dr. Sabin went East to become the first woman professor at Johns Hopkins University, Baltimore, and the first woman to be elected to a life membership in the National Academy of Sciences.

FLORIDA

Cardiovascular Seminar in St. Petersburg.—The annual Suncoast and Hillsborough County Cardiovascular Seminar will be held Friday and Saturday, April 3 and 4, at the Tides Hotel and Bath Club, Redington Beach, St. Petersburg. Programs will be presented from 10 a. m. to 5 p. m. each day. This seminar is sponsored jointly by the Suncoast Heart Association, St. Petersburg, and the Hillsborough County Heart Association, Tampa. Seven specialists in various phases of diagnosis, treatment, and surgery in the cardiovascular field will present papers and take part in panel discussions, including Dr. John W. Hurst, Emory University; Dr. John B. Hickam, University of Indiana; Dr. Haddow M. Keith, University of Toronto Medical School; and Dr. Herbert E. Warden, University of Minnesota, Minneapolis. Credit for attending the seminar will be given by the American Academy of General Practice and the sponsoring heart associations cordially invite all physicians to attend. Registration fee

is $5. For information, write the Hillsborough County Heart Association, 111 Zack St., Tampa 2, Fla.

IDAHO

Cancer Conference in Boise.—The first annual Idaho Cancer Conference of the American Cancer Society, Idaho Division, will be held in Boise April 10-11 at the Hotel Boise, with physicians, dentists, and nurses participating. Of the six sessions scheduled, the following will be for physicians only, with Dr. Frank W. Crowe, Portland, Ore., presiding:

Diagnosis and Treatment of Cancer of the Uterus, Dr. John A. Wall, Houston, Texas.
Current Problems with Cancer; Polyps of the Colon and Rectum, Dr. Joel W. Baker, Seattle.
Breast Cancer—Treatment, Dr. Frank E. Adair, New York City.
Question-Answer session.
Conclusion, Dr. Crowe.

For information write Dr. Crowe at 116 W. State St., Boise, Idaho.

LOUISIANA

Appoint Dr. Beaver to Professorship.—Paul C. Beaver, Ph.D., was appointed the William Vincent Professor of Tropical Diseases and Hygiene at Tulane University School of Medicine, New Orleans. Dr. Beaver, formerly professor of parasitology, was a member of the medical school faculty since 1945. He succeeds Ernest Carroll Faust, Ph.D., who has reached retirement age but continues as field coordinator of the Tulane consultant program with the seven medical schools of Colombia, South America.

Personal.—Dr. Charles E. Dunlap, chairman, department of pathology, Tulane University School of Medicine, New Orleans, was reelected to a new three-year term on the Board of Directors of the Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn. The council of the institute at its annual meeting Oct. 21 also elected Fisk University, Nashville, as its 37th sponsoring university.—Dr. William W. Frye, dean and professor of tropical medicine, Louisiana State University School of Medicine, New Orleans, was appointed to the National Advisory Allergy and Infectious Diseases Council. Since 1946, Dr. Frye has been a special consultant in tropical medicine to the U. S. Public Health Service.

MASSACHUSETTS

Dr. Jailer to Lecture.—The Alpha Omicron chapter of the Phi Delta Epsilon Fraternity will hold its Aaron Brown lectureship series April 3 in the Boston University School of Medicine auditorium. The guest speaker will be Dr. Joseph W. Jailer, department of medicine, Columbia University College of Physicians and Surgeons, New York City. His subject is "Certain Aspects of Hyperadrenalism."

MICHIGAN

Establish Residents' Day for Obstetrics-Gynecology.—An annual "Residents' Day" was established by the department of obstetrics and gynecology at Wayne State University College of Medicine, and the first program was held Feb. 25. All residents in obstetrics and gynecology in Michigan are invited to attend these one-day sessions held at the Wayne County Medical Society auditorium. Dr. Clyde L. Randall, chairman of obstetrics and gynecology, University of Buffalo College of Medicine, was the dinner speaker Feb. 26. Dr. Randall spoke on the "Oophorectomy and the Consequences." During afternoon ward rounds at Receiving Hospital, there was a brief presentation on the "Current Treatment of Pelvic Inflammatory Disease."

Mortality in Child Birth.—The rate at which Michigan women die as a result of childbirth or pregnancy was reduced by 67% in the last 10 years, according to figures released by the Michigan Department of Health. In 1947, 11 Michigan mothers died for every 10,000 babies born alive. In 1957, the rate was 3.8. Provisional figures for the first nine months of 1958 indicate the rate for last year will be below the 1957 figure. To stress the importance of early prenatal care, classes for expectant parents are conducted in 34 Michigan counties. Dr. Charles A. Behney, maternal and child health consultant, Michigan State Health Department, said major causes of maternal deaths today are hemorrhage, toxemia, infection, anesthesia, and heart disease.

Support for Survival Proposition.—Dr. George Moore, regional medical officer, Office of Civil and Defense Mobilization, Battle Creek, announced that "Michigan voters should support Proposition 1 on the state ballot April 6 to assure the survival of the state's government in the event of nuclear attack. Proposition 1 simply modernizes our present Michigan laws so that governments at all levels can carry out their responsibilities to assure the continuity of civilian government . . . judicial, legislative and executive . . . and the continuation of civil law in the event of a nuclear attack. Under this law, the Legislature can provide succession in office, if incumbents are disabled by enemy attack, and can adopt such other measures at county and city levels as is deemed necessary to assure that individual liberties and civil rights of the people will be preserved and protected following an enemy attack upon this Nation. If the amendment is approved by the voters it also provides that elections shall always be called, as soon as possible, to fill any elective vacancies, in any offices, temporarily occupied, due to the incapacity of the lawful elected officials. In effect, the law prepares for continuation of civilian law and order to prevent martial or dictatorial law in time of nuclear war."

MISSOURI

Dr. Wood to Give Annual Lecture.—Dr. W. Barry Wood Jr., vice-president, Johns Hopkins Medical Institutions, Baltimore, will deliver the ninth annual Memorial Lecture at the Menorah Medical Center of Kansas City on Tuesday, May 12. The subject of his lecture will be "The Genesis of Fever." Dinner will be at 6:30 p. m. and the lecture at 8 p. m.

NEW MEXICO

Devote Annual Meeting to Space Medicine.—The annual meeting of the New Mexico Medical Society in Las Cruces, May 5-7, will be devoted exclusively to space medicine, Dr. James C. Sedgwick, president, has announced. A tour and demonstration will be held May 5 at Holloman Air Base, N. M., a few miles from Alamogordo, where the Air Force Missile Development Center, Air Research and Development Command of the U. S. Air Force is located. Sessions on May 6 and 7, held in Milton Hall at New Mexico State University, Albuquerque, will include discussions by guest speakers on research problems in space medicine. Physicians will witness the routine operation of missile testing and may see missiles fired. The following are scheduled to discuss the subjects listed:

Dr. W. Randolph Lovelace, II, Albuquerque, "Crew Selection for Space Flight"; Col. John Pickering, Randolph Air Force Base, San Antonio, Texas, "Radiation Problems in Space Medicine"; Col. John Paul Stapp, Wright Air Development Center, Ohio, "Accelerations in Space Flight"; Major Stanley C. White, Washington, D. C., "Cabin Ecology for Space Flight"; and Capt. George E. Ruff, Wright Air Development Center, Ohio, "Psychophysiology of Space Flight."

Also present will be Dr. F. J. L. Blasingame, Executive Vice-President of the American Medical Association. The Air Force requires that all who plan to go on the conducted tour must preregister by April 15 to be cleared through security. All who have a registration badge will be permitted to board the Air Force buses for the tour, including wives, exhibitors, and guests. The Air Force will not permit private automobiles or cameras. Mail advance registration, with registration fee of $10, to New Mexico Medical Society, 220 First National Bank, Albuquerque, N. M. Room reservation information will be mailed to those who forward registration.

NEW JERSEY

Orthopedic Seminar.—The orthopedic department of St. Joseph's Hospital, Paterson, will hold an orthopedic seminar designed only for residents in orthopedic surgery on Saturday, April 4. Residents who are being trained in New England, New York, New Jersey, Pennsylvania, Delaware, Maryland, and in the District of Columbia are cordially invited. There is no charge. Advance registration is requested. Please address all communications to Dr. R. R. Goldenberg, St. Joseph's Hospital, Paterson, N. J.

NEW YORK

Meeting on Tuberculosis and Health—The annual meeting of the New York Tuberculosis and Health Association, Inc., will be held April 8 at the Hotel Statler Hilton, New York City. Moderator for the scientific and sociologic session will be Dr. John H. McClement, visiting physician-in-charge, chest service Bellevue Hospital. Papers to be presented include:

Tuberculosis Among the Navajo: Research in Cross-Cultural Technologic Development in Health, Dr. Kurt W. Deuschle, Cornell University Medical College.

The Tuberculin Test: An Old Test with a New Look, Dr. Michael L. Furcolow, Kansas City Field Station, U. S. Public Health Service.

Some Observations on the Use of Drugs in the Prevention of Experimental Tuberculosis (Chemoprophylaxis), Dr. Leon H. Schmidt, Christ Hospital, Cincinnati.

At the luncheon session, Dr. Carl Muschenheim, president of the association, will speak, and Dr. Walsh McDermott, Livingston Farrand Professor of Public Health and Preventive Medicine, Cornell University Medical College, will present "The Community's Stake in Medical Research."

Institute on Medical Teaching.—The second Summer Institute on Medical Teaching, jointly sponsored by the University of Buffalo and the Association of American Medical Colleges, will be held in Buffalo June 9-18, 1959. Included in the presentations, demonstrations, and discussions led by University of Buffalo faculty from the schools of medicine, education, and arts and science will be such topics as the nature of learning; the nature of medical students and medical faculties; the philosophical background for higher education in the United States; the use of lecture and laboratory, ward exercise, and clinical conference, as well as less familiar methods of instruction; and the use of tests and other appraisal devices for measuring student performance in a medical school. Opportunity for consultation on individual instructional problems will also be provided. Attendance will be limited. Interested members of Medical School faculties in the United States and Canada may apply for registration or information by writing Dr. George E. Miller, associate professor of medicine, University of Buffalo School of Medicine, Buffalo 14, N. Y.

New York City

Dr. Wilson Wins Prize in Neurology.—Irwin B. Wilson, Ph.D., associate professor of biochemistry, Columbia University, was awarded the annual prize in neurology given by the Association for Research in Nervous and Mental Disease. The prize carries

an award of $1,000. Dr. Wilson recently achieved national recognition for his success at designing PAM, antidote against the toxic effects of nerve gas and insecticides. The citation issued by the association commended Dr. Wilson for his antidote and for his "contribution toward man's understanding of the action of toxic gases on the nervous system."

Doctors' Symphony Gives Benefit Concert.—The Brooklyn Doctors' Symphony Orchestra, of which Maurice P. Yuppa, D.D.S., is president, presented a concert on Feb. 20 for the benefit of Student Nurses recruitment program of the Nurses Association of the Counties of Long Island. Physicians, dentists, nurses, and members of allied professions are invited to become members of the orchestra. Rehearsals are held at 8:30 p. m. at The Clara Barton Vocational High School, 901 Classon Ave., Brooklyn. For details contact Dr. Benjamin A. Rosenberg, 909 President St., Brooklyn 15 (Nevins 8-2370).

Vitamin Researcher Celebrates Seventy-Fifth Birthday.—Dr. Casimir Funk, pioneer in vitamin research, marked his 75th birthday Feb. 23. Dr. Funk was born in 1884 in Warsaw, Poland, son of a dermatologist. He received his Ph.D. in organic chemistry from the University of Berne. He then went to the Pasteur Institute in Paris to work with Gabriel Bertrand, reportedly the first professor of biochemistry. At the Lister Institute in London, in 1911, Dr. Funk isolated from rice polishings a substance that cured beriberi. Knowing this substance essential to life, he gave it the name "vitamine," later changed to vitamin. Shortly thereafter, he isolated crystalline nicotinic acid and other vitamin B components from extracts of yeast and rice polishings, and worked out the manner in which thiamine (vitamin B_1) is utilized by the body. In 1923, Dr. Funk was appointed by the Rockefeller Foundation to organize the department of biochemistry at the State School of Hygiene in Warsaw. Since 1947, Dr. Funk and his co-workers at the Funk Foundation for Medical Research, a nonprofit organization, have been engaged in basic research on problems of cancer, diabetes, peptic ulcer, and arthritis.

OREGON

University Gets Million-Dollar Gift.—The University of Oregon Medical School will share equally with Good Samaritan Hospital, Portland, in the proceeds of an estate valued at 2 million dollars, Dr. David W. E. Baird, dean, has announced. The money, from the estate of the late Arthur H. Devers, is mostly in stocks and bonds, with about $100,000 in cash and mortgages. According to the terms of the will, Dr. Baird said, half of the funds, upon the death of Mr. Devers' widow, were to be turned over to the Oregon State Board of Higher Education for the purpose of teaching the subjects of eye, ear, nose, and throat at the University of Oregon Medical School. Mr. Devers, a coffee roasting pioneer, died Sept. 15, 1944. Upon his death a certain number of specific bequests were made and the residue of the estate was held in trust until the death of his widow, Mrs. Anne E. Devers, recently.

PENNSYLVANIA

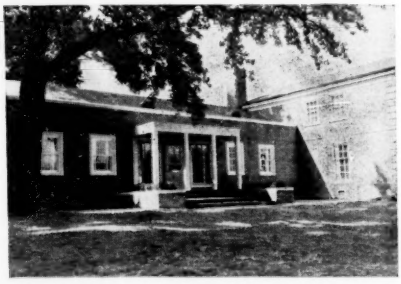
Plan New Hospital in Media.—Directors planning the new Riddle Memorial Hospital near Media announced the appointment of a Doctor's Advisory Committee, composed of physicians serving on the staffs of other hospitals and clinics in the Philadelphia area. Riddle Memorial will be built largely from funds bequeathed for this purpose by the late Samuel D. Riddle, race-horse owner. It will be built on a 72-acre plot left by Mr. Riddle on Baltimore Pike near Media, to serve the 75,000 people of Central Delaware County. Long range plans include the erection of a modern 150-bed hospital, expandable to 300 beds, a nurses home, doctors offices, and a geriatrics center for research and study in connection with the rapidly growing elderly section of the American population. Cost of the main building, planned to be started in 1960, will be about 5 million dollars.

Philadelphia

Open Laboratory of Cytology.—A symposium on cytology was held Feb. 27 at the Hahnemann Medical College to mark the opening of the new Laboratory of Cytology. The following five pathologists spoke at the symposium: Dr. Cyrus C. Erickson, professor of pathology, University of Tennessee, Memphis; Dr. Irene Koprowska, director, Hahnemann Cytology Laboratory; Dr. Peter A. Herbut, of Jefferson Medical College; Dr. Emerson Day, director, Strang Cancer Prevention Clinic of Memorial Hospital, New York City; and Dr. James W. Reagan, Western Reserve University School of Medicine, Cleveland. Under Dr. Koprowska's direction, the Cytology Laboratory is engaged in a four-fold program. The diagnostic service examines body fluids and secretions for cancer cells. The laboratory is one of about 30 in the country recognized as a teaching center to train pathologists and technicians, and is approved by the Board of Schools of Medical Technologists of the American Society of Clinical Pathologists. The laboratory has been conducting research concerned with chemically-induced cervical carcinoma of mice. In a program supported by the U. S. Public Health Service, it also participates in a cooperative pilot study of the American Cancer Society and the Veterans' Administration concerned with a simultaneous mass population screening by cytologic and radiologic methods for the early detection of cancer of the lung.

VIRGINIA

New Headquarters Building for State Society.—The Medical Society of Virginia recently held an open house in dedication of its new headquarters building at 4205 Dover Road, Richmond. In 1946 the society expanded its work with the employment of the late Mr. Henry S. Johnson as director of public relations and the need for more adequate work space for society executives was apparent. In 1951, a building was purchased at 1105 W. Franklin St., which became the society's official headquarters. Subsequently, a study committee with Dr. Guy W. Horsley, as chairman, recommended that a new headquarters building be erected. This action was approved by the council, the House of Delegates, and the membership at its annual convention in 1956. The maximum sum of $120,000 was appropriated for purchase of the land, erection of the building, and for equipment. A building committee appointed by President James Hagood began its work on Oct. 31, 1956. The present property was



The new headquarters building of the Medical Society of Virginia located in Richmond.

acquired from the Richmond Foundation. The new building was completed in September, 1958, and contains a reception area, committee meeting rooms, executive offices, a small kitchen, a conference room, offices where the *Virginia Medical Monthly* work is done, and, on the second floor, the office of the Virginia Academy of General Practice. The land for the building cost $21,000 and the building itself cost $80,000. The total cost including architect's fees, equipment, etc., was just under $116,000. An off-street parking area in front of the building can accommodate 200 cars.

GENERAL

Fellowships in Audiology and Speech.—Opening of competition March 6 for two fellowships in audiology and speech at Northwestern University, Chicago, has been announced by the American Hearing Society, its member agency, the St. Paul Hearing Society, and the university. Winners of the awards, known as the Reine Humbird Myers Fellowships, will receive $3,000 a year for two years while participating in a graduate program in preparation for work in local hearing societies. The fellowships were established in 1957 through a bequest from the Myers Foundation of St. Paul, Minn. Information and applications may be obtained from Crayton Walker, executive director, American Hearing Society, 919 18th St., N. W., Washington 6, D. C. Closing date for returning completed applications to Mr. Walker is April 6.

Biennial Conference on Anesthesiology.—"The Heart and Anesthesia" is the theme for the sixth biennial Western Conference on Anesthesiology to be held April 1-4 at the Westward Ho Hotel, Phoenix, Ariz. The conference will open with an address by Dr. Daniel C. Moore, Seattle, president, American Society of Anethesiologists. The following panel discussions and moderators are planned:

Applications to Clinical Anesthesia, Dr. Stuart C. Cullen, San Francisco.
Practical Use of Monitory Devices—Which, When, How, To Whom?, Dr. Robert D. Dripps, Philadelphia.
The Unsolved Problems of Cardiac Surgery, Dr. Robert W. Virtue, Denver.

A motion picture, "Fluothane," will be shown each day. Entertainment will include tours, golf, swimming, horseback riding, and a ladies' program.

Meeting on Border Public Health.—The United States–Mexico Border Public Health Association will hold its 17th annual meeting in Brownsville–Matamoros, March 30-April 3. During the plenary sessions there will be discussions on the recent progress in public health both in the U. S. and in Mexico, the activities of joint health councils in border communities, the epidemiology and laboratory aspects of arthropod-borne encephalitides, the needs and resources for the training of public health personnel working along the border, the rabies problem in the border area, and the attenuated live poliovirus oral vaccine. Six sessions (maternal-child health, veterinary public health, venereal diseases, nursing, sanitation, and tuberculosis) will meet, some of them in joint meetings. Simultaneous interpretation services will be available in all plenary sessions. For information write the United States–Mexico Border Public Health Association, 243 U. S. Court House, El Paso, Texas.

Psychotherapy Meeting in San Francisco.—The fifth annual Western regional meeting of the American Group Psychotherapy Association will be held April 2-3 in San Francisco at the Sheraton–Palace Hotel. Advances the past year in group psychotherapy will be keynoted in a paper by Dr. Martin Grotjahn, of Beverly Hills, with Mr. S. R. Salvson, of New York City, editor of the *International Group Psychotherapy Journal*, as discussant. More than 17 symposiums, workshops, and general sessions will

consider group counseling in a state prison, group therapy programs for family agencies, group psychotherapy for criminal offenders, family group therapy, therapeutic techniques in adolescents' groups, the transactional analysis, treatment of psychotic patients by group methods, and allied subjects. The meeting arrangements are in charge of Dr. Hymen S. Morgenstern, of San Francisco, and Dr. Max A. Sherman, of Beverly Hills, co-chairmen. For information, write Dr. Donald A. Shaskan, VA Mental Hygiene Clinic, 49 Fourth St., San Francisco 3.

Study of Hospital Admissions.—The reason more than 20 million Americans—about 12.5%—enter a hospital each year will be the subject of a study authorized by the executive committee of Health Information Foundation. It will be conducted jointly by the National Opinion Research Center of the University of Chicago and the foundation. A sample of admissions to hospitals in Massachusetts will be examined through the approval and cooperation of the Massachusetts Medical Society, the Massachusetts Hospital Association, and the Blue Cross–Blue Shield Plans in that state. The 2½-year study will attempt to ascertain the nonmedical factors and family situations which lead to hospital utilization as well as medical reasons given by physicians. The survey is one of a group of major studies of voluntary health insurance sponsored by the foundation. The foundation was organized in 1950 as a contribution by the drug, pharmaceutical, chemical, and allied industries to research and education in the social and economic aspects of medical care.

Centennial for Section on Obstetrics and Gynecology.—The Section on Obstetrics and Gynecology of the American Medical Association will commemorate the 100th anniversary of its founding at the A. M. A. meeting in Atlantic City, June 8-12. A special program is being arranged for this occasion, including a commemorative luncheon and an address by Mr. Andrew Claye, of Leeds, England, president of the Royal College of Obstetricians and Gynecologists of Great Britain. Also included are a panel discussion on "Pelvic Exenteration—Current Status" on June 10; a combined meeting June 11 of seven A. M. A. Sections (Pathology and Physiology, Pediatrics, Nervous and Mental Diseases, Anesthesiology, Diseases of Chest, General Practice, Obstetrics and Gynecology) considering "Childbirth—Progress in Management"; June 12, a joint meeting with the Section on Pathology and Physiology, including two panels, "Ovarian Tumors" and "Rh Disease." Hotel reservation forms for this meeting will appear in THE JOURNAL or can be obtained from A. M. A. headquarters, 535 N. Dearborn St., Chicago 10.

Conference on Municipal and Industrial Waste.—The eighth Southern Municipal and Industrial Waste Conference will be held April 2-3 at the University of North Carolina, Chapel Hill. These conferences, organized jointly by Duke University, North Carolina State College, and the University of North Carolina, are for the purpose of bringing together representatives of industry, municipalities, and governmental agencies responsible for developing policies relating to the preservation of water resources in the southeastern part of the U. S. The eighth conference will be devoted to techniques available in the treatment of municipal and industrial waste waters. General sessions will be devoted to "solids separation processes," "chemical and biological treatment," and "solids handling and disposal." Formal papers will be followed by prepared discussions and by an informal discussion. Registration fee is $15 and includes attendance at all sessions, a copy of the conference *Proceedings*, two luncheons, and the social hour and banquet. For information write the University of North Carolina School of Public Health, Department of Sanitary Engineering, Chapel Hill, N. C.

Meeting on Physical Medicine in New Haven.—The Eastern Section of the American Congress of Physical Medicine and Rehabilitation will meet April 18 at the Yale University School of Medicine, New Haven, Conn. The program includes the following:

Connective Tissue Massage, Dr. Morton Hoberman, New York City.
Stretching, Dr. Thomas F. Hines, New Haven.
Proprioceptive Facilitation, Dr. Herman Kabat, Providence, R. I.
First Publications in Physical Medicine, Dr. John F. Fulton, New Haven.
Comparative Values of Electrodiagnosis and Electromyography, Dr. W. T. Liberson, Chicago.
Skin Thermometry in the Diagnosis of Peripheral Vascular Diseases, Alfred Ebel, New York City.
Importance of Leg Length in Low Back Pain, Dr. Harold Lefkoe, Philadelphia.
The Third International Congress of Physical Medicine, Dr. Frank H. Krusen, Rochester, Minn.
Trends in Medical Education, Dr. Vernon S. Lippard, dean, Yale University School of Medicine.

Parts of the program will be chaired by Drs. Robert C. Darling, of New York City, and Ernst Fischer, of Richmond. For information write Dr. Sidney Lich, 360 Fountain St., New Haven 15, Conn., secretary.

General Practice Meeting in San Francisco.—The American Academy of General Practice will hold its 11th annual scientific assembly April 6-9 in San Francisco's Civic Auditorium. The scientific program will feature 28 physician-speakers. More than 100 scientific and 300 technical exhibits are planned. The Congress of Delegates will convene at 2 p. m., April 4, in the Fairmont Hotel. Opening ceremonies at 1 p. m., April 6, include a call to order by Dr.

Holland T. Jackson, Fort Worth, Texas, president of the academy. Dr. Walter H. Judd, U. S. Congressman from Minnesota, will speak on "Doctors in a Changing World." Other participants include Dr. Leroy E. Burney, surgeon general, U. S. Public Health Service, presenting "Public Health: Its Relation to the Practice of Medicine," and James H. Steele, D.V.M., U. S. Public Health Service, who will give "Animal Diseases Transmissible to Man." The president's reception is planned for the evening of April 8. A ladies' program is arranged, and postassembly plans include the Invitational Scientific Congress April 13-14 in Honolulu, Hawaii. For information write The American Academy of General Practice, Volker Boulevard at Brookside, Kansas City 12, Mo.

Pediatricians Meeting in San Francisco.—The American Academy of Pediatrics will hold its spring session at the Sheraton-Palace Hotel, San Francisco, April 13-15. The general sessions and exhibits will be held at the hotel, and afternoon clinics will be conducted in four of the pediatric departments in the Bay Area, April 15. A "Conference on Respiratory Problems of the Newborn" will be moderated by Dr. Moses Grossman, San Francisco, April 13. The following panel discussions and moderators are scheduled:

Inborn Errors of Metabolism, Dr. Ruth Gross, San Francisco.

Some Current Problems in Infectious Diseases, Dr. Henry B. Bruyn, San Francisco.

Problems in Growth and Development, Dr. Donald Pickering, Portland, Ore.

Abdominal Surgical Problems in Pediatrics, Dr. Edward B. Shaw, San Francisco.

Adolescence—The Pediatrician's Problem, Dr. Arthur Roth, Oakland.

Clinical Pediatric Allergy, Dr. John P. McGovern, Houston, Texas.

Entertainment includes the banquet April 14, 8 p. m. ($7.50), and a ladies' program. For information write the American Academy of Pediatrics, P. O. Box 1116, Evanston Ill., Dr. E. H. Christopherson, Executive Secretary.

Meeting on Sterility in Atlantic City.—The 15th annual meeting of the American Society for The Study of Sterility will be held at the Shelburne Hotel, Atlantic City, N. J., April 3-5. The secretary of the society is Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham 5, Ala., and the president of the society for 1959 is Dr. Edward C. Reifenstein Jr., New Brunswick, N. J. On April 3 the Squibb prize paper from the 1958 annual meeting of the Pacific Coast Fertility Society, "The Endocrine Control of the Passage of Spermatozoa and of Ova Through the Female Genital Tract," will be given by Dr. Robert W. Noyes, department of obstetrics and gynecology, Stanford University School of Medicine, San Francisco. On April 5 Dr. Peter M. F. Bishop will give the Ayerst Lecture, "Cervical Mucus." Dr. Bishop is from the department of obstetrics and gynaecology, Postgraduate Medical School, Guy's Hospital, and Chelsea Hospital for Women, London, England. The presidential address, "Nolle Nodere," will be presented by Dr. Sheldon A. Payne, The Shelton Clinic, Los Angeles, and the Fred A. Simmons Memorial Address, "Experience, Experiment, and Error in Sterility," by Dr. Alan N. B. Grant, department of gynaecology, Women's Hospital, Sydney, Australia.

Neurology Meeting in Los Angeles.—The 11th annual meeting of the American Academy of Neurology will be held April 13-18 at the Statler-Hilton Hotel, Los Angeles, under the presidency of Dr. Francis M. Forster, Madison, Wis. Special courses will be conducted April 13-15. The S. Weir Mitchell Award Essay is scheduled for the morning session of April 16. Papers to be presented by foreign participants are as follows:

Some Features of the Pathogenesis of Myotonia, N. I. Grashchenkov, Moscow, U.S.S.R.

Electrophysiological Study of Cortical and Spinal Cord Lesions in Cats with Allergic Encephalomyelitis, Roger M. Morrell, Montreal, Quebec.

Injury to the Nervous Tissue Produced by Intracarotid Injection of Alcohol, J. Olszewski and B. Rozdilskyi, Saskatoon, Saskatchewan.

Electron Microscope Study on the Function of Astroglia in the Water Ion Metabolism of the CNS, H. M. Gerschenfeld, F. Wald, J. A. Zadunaisky, and E. De Robertis, Buenos Aires, Argentina.

A symposium on rhinencephalon the morning of April 17 will have Dr. Ray S. Snider, of Chicago, as chairman. A joint meeting of the sections of neurochemistry and neuropharmacology will be held. Eighty-six papers are scheduled for presentation at the scientific sessions, and over 70 papers will be read by title. Scientific, society, and commercial exhibits and demonstrations and movies are planned. For information write the American Academy of Neurology, 4307 E. 50th St., Minneapolis 17.

Fellowships for Study of Human Ecology.—A grant from the estate of Anne Parrish Titzell, professor of medicine (neurology), Cornell University Medical College, New York City, made possible the establishment of fellowships for those interested in the study of human ecology and its relation to health. An immediate purpose is to provide opportunities for study and investigation for men who plan to pursue academic careers. Three general areas are within the scope of the program: the investigation of the social and physical milieu in which men live, and the attempt to learn more about how specific aspects of this milieu affect health and behavior; the investigation of the interaction between men and their milieu, and of how a man's perception of his life situation influences his reaction to it; the investigation of the interac-

tion between bodily processes and the highest integrative activities of the brain, and the relevance of this to specific disease syndromes. Dr. Lawrence E. Hinkle Jr. will be associated with Dr. Harold G. Wolff in the direction of the program. The staff includes representatives from internal medicine, psychiatry, neurology, psychology, sociology, and cultural anthropology. Fellows will have an opportunity to participate in field observations of groups drawn from the general population, to take part in the long-term observation and care of out-patients in a research facility especially designed for this purpose, and to make use of laboratory facilities for the study of behavior, and of processes relating to the functions of various organ systems. Three fellowship appointments will be made annually each for a term of two years. Applicants should have completed one or more years of postgraduate training in the fields of internal medicine, neurology, psychiatry, preventive medicine, or public health. The stipend allowed is $4,500 the first year, and $5,000 the second; an additional allowance of $500 per annum is made for each dependent. To make application, write to Dr. E. Hugh Luckey, Chairman of the Department of Medicine, New York Hospital–Cornell Medical Center, 525 E. 68th St., New York 21.

CANADA

Surgeons Meet in Montreal.—A sectional meeting of the American College of Surgeons will be held April 6-9 at the Queen Elizabeth Hotel, Montreal. More than 15 symposiums are planned, and the following panel discussions and moderators are scheduled:

Biliary Tract Surgery, Dr. Richard B. Cattell, Boston.
Discussion on Activities of the College, Dr. Paul R. Hawley, Chicago, director of the college.
Angioplastic Procedures in the Management of Peripheral Arterial Occlusive Disease, Dr. D. Emerick Szilagyi, Detroit.
Anesthesia for Surgery, Dr. Louis Lamoureux, Montreal.
Medicolegal Aspects of Trauma, Dr. Alexander P. Aitken, Boston.
Cardiovascular Surgery, Dr. David R. Murphy, Montreal.
Fractures of Neck of Femur, Dr. J. Gordon Petrie, Montreal.

Dr. L. G. Stevenson, dean, Faculty of Medicine, McGill University, will present an address at the dinner of the Montreal Ophthalmological Society, 7 p. m., April 6. A round-table conference on detachment of the retina will be moderated by Dr. Samuel T. Adams, Montreal, April 7. At the college dinner 7 p. m., April 8, with Dr. Newell W. Philpott, Montreal, president of the college, presiding, Mr. Hugh MacLennan, Montreal, will be the speaker. Section meetings, motion pictures, and exhibits are arranged.

LATIN AMERICA

Nutrition Institute Founded in Mexico City.—A new, autonomous National Institute of Nutrition, comprising the Hospital for Nutritional Diseases, the Directorate of National Nutrition, and a Division of Research and Training, was organized by the government of Mexico. To help support research in biochemistry and nutrition at the institute, the Rockefeller Foundation appropriated $90,000 for use over a three-year period. The Hospital for Nutritional Diseases, established in the early 1940's, has contributed to medical training and research and to hospital care in Mexico. The Directorate of National Nutrition is responsible for community and public health aspects of nutrition. Studies undertaken by the directorate are being supported by the Mexican Department of Health with assistance received under a cooperative agreement with the World Health Organization, the United Nations International Children's Emergency Fund, and the Food and Agriculture Organization. The chief unit of the Division of Research and Training is the department of biochemistry. A staff, headed by Dr. Guillermo Soberon, has been formed, and a two-year course leading to the National University of Mexico's master's degree has been started. Initially, the biochemical research will focus on three main topics: the development of better methods for determining nutritional status; the nutritional value of Mexican foods; and protein metabolism, including the utilization of proteins and amino acids in Mexican foods.

FOREIGN

Spain's "Oldest Doctor" Dies.—The San Antonio *Light* reported that Dr. Jose Amo Serrano, reportedly Spain's oldest doctor, died in Cordoba, Spain, Jan. 9. Dr. Serrano had remained active in his profession until he was 100.

British and Irish Surgeons Meet in London.—The annual meeting of the Association of Surgeons of Great Britain and Ireland will be held April 23-25 in London under the presidency of Prof. Sir James Paterson Ross with the following papers scheduled:

Acute Pancreatitis.
Clinical Diagnosis in Chronic Pancreatitis.
Chronic Pancreatitis.
Islet-cell Tumors of the Pancreas.
Genito-urinary Tuberculosis.
Bone Tuberculosis.
Tuberculous Lymphadenitis.

A Moynihan Lecture at the Royal College of Surgeons will follow an afternoon of films, April 24, on which evening will be held the annual dinner. The Honorary Secretary of the Association is Mr. Rodney Smith, 47 Lincoln's Inn Fields, London, W. C. 2.

British Association for Medical Education.—The Association for the Study of Medical Education in Great Britain, organized late in 1957 to serve as a forum for persons interested in the problems of

medical education and as a clearinghouse for information on the field, will be assisted during its initial, developmental years by a grant of £10,000 (about $28,500) from the Rockefeller Foundation to the Royal College of Physicians, London. The major purposes of the association are to exchange information on medical education in Great Britain, organize meetings on relevant topics, maintain a bureau where information can be received, stored, and made available to those interested, and encourage, promote, or conduct research into matters concerned with medical education. It is free to initiate other activities which it decides will advance the interests of medical education. Almost all the licensing bodies and medical schools of Great Britain, as well as individual medical educators and practitioners, are members of the new association.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Phoenix, April 5-10. Applications now on file. *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application was Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Philadelphia, June 2-6; St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 5-9. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Boston, April 16-19. Final date for filing application was Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application was February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Public Health.* Minneapolis, Boston, Baltimore, Chapel Hill, North Carolina and New Orleans, April 9-11; Berkeley, Calif., April 23-25; Pittsburgh, April 16-18. *Occupational Medicine.* Chicago, April 24-26. *Aviation Medicine.* Los Angeles, April 24-26. Final date for filing all applications is March 16. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written.* Philadelphia, September. Final date for filing application is March 15. Sec., Dr Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: *Written.* Various centers throughout the country, September 1959. Final date for filing application is July 1. *Oral.* September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

AMERICAN BOARD OF UROLOGY: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

NAVY

Captain Schiff Honored.—Capt. Maurice Schiff, chief of the eye, ear, nose, and throat service at the U. S. Naval Hospital, Oakland, Calif., was selected as the 1959 recipient of the Harris P. Mosher Memorial award, an honor that comes in connection with his election to active fellowship in the American Laryngological, Rhinological, and Otological Society, Inc. The organization confers this honor each year on the candidate who submits the best thesis. "Juvenile Nasopharyngeal Angiofibroma" was the title of Captain Schiff's thesis. Dr. Schiff presented his paper at the annual meeting of the society in Hot Springs, Va., on March 12. The honor carries with it a Harris P. Mosher Memorial award certificate, the listing of the recipient's name on the scroll published each year in the annual program of the society, 100 complimentary copies of the prize thesis, and its submission for consideration for publication in a forthcoming issue of *Laryngoscope*.

PUBLIC HEALTH SERVICE

Research Training Program.—Seventeen countries of Central and South America and Australasia will participate in the Public Health Service's international research training program. The program, which was started a year ago, provides medical research training in the United States for scientists from abroad. With the 17 new participants (Argentina, Australia, Brazil, Ceylon, Chile, Columbia, El Salvador, India, Iran, Japan, Mexico, New Zealand, Pakistan, Peru, Philippine Islands, Thailand, and Uruguay), 30 countries are now participating in the program. A research fellowship review panel of scientists has been established in each country. Within each nation, candidates are nominated by its scientific panel, and final recommendations for the awards from the Public Health Service are made by a research fellowship board of the National Institutes of Health.

The chairman of the fellowship board is Dr. John R. Paul, professor of preventive medicine at Yale University, who, with Dr. Ronald E. Scantlebury of the National Institutes of Health, served as advisor to the participating countries in setting up their review panels and in entering the program. In 1958, through similar panels, applications resulting in 17 awards were received from Austria, Belgium, Denmark, England, Finland, France, Germany, Holland, Italy, Norway, Spain, Sweden, and Switzerland. The 17 research fellows are now doing research in medical centers in the United States. Each fellow holds a doctoral degree or its equivalent in one of the medical or related sciences and has demonstrated promise in research. All have a workable knowledge of English. The training of these scientists from other countries will strengthen medical research throughout the world and will give outstanding scientists a chance to share knowledge with kindred groups by conducting research in the United States. Under the program, the Public Health Service provides a basic annual stipend of $4,500, allowances for wives and children, and limited travel funds. Information about the program may be obtained from Dr. Ronald E. Scantlebury, Chief, Foreign Grants and Awards, Division of Research Grants of the National Institutes of Health, Bethesda 14, Md.

New Publications.—A monograph entitled "Morbidity from Cancer in the United States" (PHS publication no. 590) by Harold F. Dorn, chief, Biometrics Branch, Division of Research Services, National Institutes of Health, and Sidney J. Cutler, Head, Clinical Biometry Section, Biometrics Branch, National Cancer Institute, is now available. Part 1 which was published separately, in 1955, deals with variations in the incidence of cancer by age, sex, race, marital status, and geographic region. The current publication completes the 10-city analysis and combines the analysis contained in part 1 with that in part 2, which deals with intercity variation in cancer incidence, trends in cancer morbidity, the association of cancer incidence and income class, and stage of disease at diagnosis. The study represents a statistical analysis of thousands of cancer cases examined in 10 large population centers in the United States which were surveyed in 1937-1939 and resurveyed 10 years later. The areas studied were Atlanta, Ga., Birmingham, Ala., Dallas, Texas, New Orleans, San Francisco, Denver, Chicago, Detroit, Philadelphia, and Pittsburgh. The book can be had by writing to the Superintendent of Documents, Government Printing Office, Washington 25, D. C. The price is $1 per copy.

The new training manual entitled "The Industrial Environment—Its Evaluation and Control" (PHS publication no. 614) is a syllabus of the short courses offered for industrial hygiene engineers and chemists at the Occupational Health Field Headquarters of the PHS in Cincinnati, Ohio. It is devoted primarily to fundamental principles and methods used in the evaluation and control of the working environment. It incorporates comprehensive reference materials, lecture outlines covering such areas as sampling analysis and engineering control measures, and laboratory exercises used in the courses. It includes a special section dealing with specific occupational health problems and their solutions. It is offered for sale by the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at $2.75 per copy.

DEATHS

Ackerman, Emma Malinda Ⓜ Sioux City, Iowa; Creighton University School of Medicine, Omaha, 1913; for many years associated with the Florence Crittenton Home; on the staffs of the Lutheran and Methodist hospitals; died Jan. 14, aged 73.

Baranco, Raymond M., Baton Rouge, La.; Meharry Medical College, Nashville, Tenn., 1912; veteran of World War I; medical director of the Southern University and Agricultural and Mechanical College; a past-president of the Louisiana Medical, Dental and Pharmaceutical Association; died in Our Lady of the Lake Hospital Dec. 19, aged 68.

Baskett, Edgar Drane Ⓜ Columbia, Mo.; Johns Hopkins University School of Medicine, Baltimore, 1919; specialist certified by the American Board of Internal Medicine; served on the faculty of the University of Missouri; formerly on the staff of the Veterans Administration Hospital in Poplar Bluff; died in Dadeville, Ala., Dec. 31, aged 67.

Bein, Philmour Murray Alexis Ⓜ Mansfield, Ohio; University of Pennsylvania School of Medicine, Philadelphia, 1932; interned at the Philadelphia General Hospital; served a residency at the Jewish Hospital in Cincinnati; veteran of World War II; specialist certified by the American Board of Surgery; fellow of the International College of Surgeons; member of the Industrial Medical association; plant physician of Westinghouse Electric Corporation and medical director of the Ingersoll-Humphreys Division, Borg Warner Corporation; associated with the People's and Madison hospitals, and the Mansfield General Hospital, where he died Jan. 9, aged 52.

Berman, Leo, Newton, Mass.; born in Brooklyn April 13, 1913; Universitat Bäsel Medizinische Fakultät, Switzerland, 1937; certified by the National Board of Medical Examiners; specialist certified by the American Board of Psychiatry and Neurology, Inc.; interned at the Lincoln Hospital in New York City; served a residency at the Bellevue Hospital in New York City, Butler Hospital in Providence, R. I., and the Boston State Hospital; member of the American Psychoanalytic Association and the American Psychiatric Association; on the faculty of Harvard Medical School in Boston, where he was on the staff of the Beth Israel Hospital; died Dec. 27, aged 45.

Bostwick, William Warren Ⓜ White Plains, N. Y.; Bellevue Hospital Medical College, New York City, 1894; veteran of World War I; died Jan. 11, aged 85.

Ⓜ Indicates Member of the American Medical Association.

Bradford, Stella Stevens Ⓜ Montclair, N. J.; Cornell University Medical College, New York City, 1902; member of the American Rheumatism Association; for many years associated with the Mountainside Hospital, where she was director of the physical medicine and rehabilitation department; died in New York City Jan. 20, aged 87.

Chilton, James C. Ⓜ Hannibal, Mo.; Beaumont Hospital Medical College, St. Louis, 1891; served as division surgeon and examiner for the Wabash Railroad and surgeon for the Chicago, Burlington and Quincy Railroad for many years; chief surgeon for the Universal Atlas Cement Company; associated with St. Elizabeth Hospital and the Levering Hospital, where he died Jan. 11, aged 92.

Collins, James Newton Ⓜ Indianapolis; Emory University School of Medicine, Atlanta, 1922; assistant professor of radiology, Indiana University School of Medicine; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, the Radiological Society of North America, and the American College of Radiology; past-secretary of the Indiana Roentgen Society; on the staffs of the St. Vincent's Hospital and the Methodist Hospital, where he died Jan. 3, aged 62.

Cooper, Harry Bryant, Mill Valley, Calif.; University Medical College of Kansas City, Mo., 1899; went to Hawaii in 1905 to attend to the medical needs of sugar plantation workers and remained in the islands for 50 years; served on Selective Service boards during World Wars I and II; died Jan. 16, aged 85.

Daly, William Harvey Jr. Ⓜ Killeen, Texas; University of Tennessee College of Medicine, Memphis, 1949; interned at Methodist Hospital in Memphis, Tenn.; formerly a resident at the Scott and White Hospital in Temple, Texas; served as vice-president of the Bell County Medical Society; associated with Burow Clinic and Hospital; died in the Scott and White Hospital in Temple Jan. 8, aged 33.

Deem, Hamlin Nichleson, Wheeling, W. Va.; Ohio Medical University, Columbus, 1901; veteran of World War I; died in the Veterans Administration Hospital, Pittsburgh, Jan. 14, aged 82.

Deruha, John, New Rochelle, N. Y.; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1920; died in New York City Jan. 16, aged 65.

De Salvo, Francis, Wausaukee, Wis.; Chicago College of Medicine and Surgery, 1917; served as health officer of Wausaukee for many years and member of the school board; at one time health officer of Niagara; died Jan. 26, aged 67.

Dozier, Joseph Vincent, Premont, Texas; Baylor University College of Medicine, Dallas, 1911; veteran of World War I; died Jan. 6, aged 82.

Elles, Norma Bertha Ⓜ Kalamazoo, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1906; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the American Ophthalmological Society; served on the faculty of Baylor University College of Medicine in Houston, Texas, where she was on the staffs of the Hermann Hospital, Memorial Hospital, and the Jefferson Davis Hospital; died in Houston, Texas, Jan. 12, aged 74.

Fasser, Alexander Otto Ⓜ Fremont, Neb.; Yale University School of Medicine, New Haven, Conn., 1905; veteran of World War I; died Jan. 14, aged 79.

Fenimore, William Nolan Ⓜ Wilmington, Del.; Jefferson Medical College of Philadelphia, 1921; veteran of World Wars I and II; served as coroner's physician; died Jan. 5, aged 72.

Hayes, Edwin Patrick Ⓜ Eau Claire, Wis.; born in Richfield Sept. 24, 1886; Marquette University School of Medicine, Milwaukee, 1913; past-president of the Eau Claire County Medical Society and the Tenth District Medical Society; served overseas during World War I; member of the American College of Obstetricians and Gynecologists and the Wisconsin Society of Obstetricians and Gynecologists; one of the founders of the Eau Claire Clinic, which was organized in 1921; on the staffs of the Luther and Sacred Heart hospitals; for 13 years director of Associated Hospital Service, Inc.; past-president of the Eau Claire Rotary Club; died in the Sacred Heart Hospital Dec. 26, aged 72.

Holland, John Gill Ⓜ Lynchburg, Va.; University of Tennessee College of Medicine, Memphis, 1933; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; president-elect of the Lynchburg Academy of Medicine; veteran of World War II; on the staffs of the Virginia Baptist, Lynchburg and Memorial hospitals; died Dec. 24, aged 56.

Horn, Dora L., Winter Park, Fla.; Cleveland Homeopathic Medical College, 1906; died Dec. 19, aged 75.

Hubbard, Milton E. Ⓜ San Francisco; University of Illinois College of Medicine, Chicago, 1928; veteran of World War II; retired from the Veterans Administration Feb. 19, 1957; died Dec. 24, aged 65.

Hutner, Louis Ⓜ Jamaica, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1934; specialist certified by the American Board of Dermatology and Syphilology; on the staff of the Queens General Hospital, where he died Dec. 15, aged 57.

Johnson, William Alexander, Reidsville, N. C.; North Carolina Medical College, Charlotte, 1907; member of the Medical Society of the State of North Carolina; died in the Moses H. Cone Memorial Hospital, Greensboro, Dec. 5, aged 76.

Keever, Henry Floyd Ⓜ Auburndale, Mass.; Harvard Medical School, Boston, 1908; associated with the Newton–Wellesley Hospital, where he served as a trustee; trustee at Lasell Junior College; died Dec. 26, aged 84.

Kells, Paul Ⓜ Miami, Fla.; University of Virginia Department of Medicine, Charlottesville, 1930; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychiatric Association; veteran of World War II; on the staffs of St. Francis Hospital in Miami Beach and Mercy and Jackson Memorial hospitals; died Dec. 29, aged 56.

Koehler, Malcolm Harvey, Newark, Ohio; Ohio Medical University, Columbus, 1900; served as county coroner; formerly a medical examiner for the Baltimore and Ohio Railroad; died Dec. 29, aged 84.

Krohn, Morris Jacob Ⓜ Denver; University Medical College of Kansas City, Mo., 1903; on the staffs of St. Joseph's Hospital and the General Rose Hospital, where he died Dec. 26, aged 80.

Lamb, Ray Floyd Ⓜ Casa Grande, Ariz.; Northwestern University Medical School, Chicago, 1947; member of the American Academy of General Practice; formerly an officer in the medical corps of U. S. Army Reserve; died Dec. 23, aged 36.

Landes, William Latimer Small Ⓜ York, Pa.; Jefferson Medical College of Philadelphia, 1916; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; veteran of World War I; an honorary member of the radiological staff of the York Hospital; on the board of directors of the Western National Bank; died Dec. 21, aged 67.

Lawn, Hugh Edward, Chicago; St. Louis College of Physicians and Surgeons, 1923; veteran of World War I; affiliated with the South Shore Hospital; died in the Veterans Administration Hospital in Hines, Ill., Dec. 22, aged 63.

Leighton, Adam Phillips Ⓜ Portland, Maine; born in Portland Jan. 23, 1887; Medical School of Maine, Portland, 1910; for many years member and secretary of the Maine Board of Registration of Medicine; past-president of the Maine Medical Asso-

ciation, Cumberland County Medical Society, and the New England Obstetrical and Gynecological Society; in 1945-1946 was president of the Federation of State Medical Boards, of which he was formerly vice-president; since 1948 a member of the National Board of Medical Examiners as a representative of the Federation, and a member of the executive committee; specialist certified by American Board of Obstetrics and Gynecology; fellow of the American Association of Obstetricians and Gynecologists and the International College of Surgeons; served as chairman of the Portland City Council and member of the Board of Alderman, and school board; veteran of World War I; in 1912 established the Dr. Leighton Private Maternity Hospital; associated with the Pownal (Vt.) State School, St. Andrews Hospital in Boothbay Harbor, Webber Hospital in Biddeford, Maine General Hospital, and the Maine Eye and Ear Infirmary, of which he was a trustee; died Dec. 26, aged 71.

McClosky, Ben Martin Ⓜ Tampa, Fla.; Ohio State University College of Medicine, Columbus, 1927; member of the American Academy of General Practice; served as city and county physician; veteran of World War II; died Dec. 10, aged 57.

McDavid, John Solomon Ⓜ Oak Park, Ill.; Northwestern University Medical School, Chicago, 1924; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; on the staffs of the Cook County and Children's Memorial hospitals in Chicago and the West Suburban Hospital, where he died Jan. 4, aged 60.

Mieczkowski, Stanislaus C., Worcester, Mass.; Maryland Medical College, Baltimore, 1912; formerly police surgeon; died in St. Anthony's Hospital, St. Petersburg, Fla., Dec. 23, aged 70.

Miller, Brownlow Bartley, Tabor, Iowa; University of Nebraska College of Medicine, Omaha, 1908; served on the staffs of the Mercy Hospital in Council Bluffs, and Bishop Clarkson Memorial Hospital in Omaha; died Dec. 22, aged 73.

Moore, Edwin Fletcher Ⓜ Cincinnati; Ohio–Miami Medical College of the University of Cincinnati, 1912; member of the American Academy of General Practice; on the staff of St. Francis Hospital; died Dec. 29, aged 69.

Moran, Michael David Ⓜ Farmington, N. M.; Washington University School of Medicine, St. Louis, 1917; veteran of World War I; died in Albuquerque, Dec. 19, aged 66.

Morrison, Whitelaw Reid, Oberlin, Ohio; Columbia University College of Physicians and Surgeons, New York City, 1914; for many years on the faculty of Oberlin College, where he was professor emeritus; at one time associated with the University of Cincinnati; for many years served as chairman of the Lorain County Health Board; taught for two years at a Chinese government school in Shanghai; joint author of "Normal and Elementary Physical Diagnosis"; died in the Allen Memorial Hospital Dec. 26, aged 72.

Motley, Robert William, Tulsa, Okla.; (licensed in Oklahoma in 1916); on the staff of the Moton Memorial Hospital, where he died Dec. 30, aged 77.

Munger, Louis P. Ⓜ Hart, Mich.; Hering Medical College, Chicago, 1895; founder of the Oceana Hospital, where he was a member of the executive board until 1956; for 12 years member of the city council; vice-president of the Oceana County Savings Bank; associated with the Oceana Canning Company of Shelby for many years, and was chairman of the board of directors; died Dec. 23, aged 85.

Myers, Thomas Ⓜ Huntington Park, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1914; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; formerly on the faculty of his alma mater and the College of Medical Evangelists in Loma Linda and Los Angeles; affiliated with Mission Hospital in Huntington Park, Los Angeles County General and the White Memorial hospitals in Los Angeles, and St. Francis Hospital in Lynwood, where he died Dec. 19, aged 67.

Nickerson, Anson LeRoy Ⓜ Kankakee, Ill.; Rush Medical College, Chicago, 1904; served as secretary of the Kankakee County Medical Society; past-president of the Kankakee County Tuberculosis Association, of which he secretary; veteran of World War I; on the staff of the Kankakee State Hospital; on the honorary staff of St. Mary's Hospital, where he died Dec. 25, aged 81.

Norviel, Herald Bernard Ⓜ Phillips, Wis.; University of Illinois College of Medicine, Chicago, 1920; past-president of the Price–Taylor Counties Medical Society; on the staff of Park Falls (Wis.) Hospital; died Dec. 7, aged 64.

Okrainetz, Clara Loewenherz Ⓜ New York City; Thüringische Landesuniversitat Medizinische Fakultät, Jena, Thuringia, Germany, 1925; specialist certified by the American Board or Radiology; member of the Radiological Society of North America and the American College of Radiology; associated with the Manhattan Eye and Ear Hospital and the Montefiore Hospital, where she died Dec. 25, aged 58.

Osheroff, Samuel A. Ⓜ San Diego, Calif.; University of Nebraska College of Medicine, Omaha, 1919; affiliated with Scripps Memorial Hospital in La Jolla; died Dec. 26, aged 70.

Paisley, Ralph Clifton, Loudonville, Ohio; Ohio State University College of Medicine, Columbus, 1930; veteran of World War II; died Dec. 24, aged 54.

Ransom, Charles Loren, Danville, Va.; born in Syracuse, N. Y., Feb. 1, 1920; Syracuse University College of Medicine, 1945; certified by the National Board of Medical Examiners; specialist certified by the American Board of Urology; vice-president of the Virginia Urologic Society; interned at St. Joseph Hospital in Syracuse, N. Y., and Johns Hopkins Hospital in Baltimore, where he served a residency in urology; served on the faculty of Johns Hopkins University School of Medicine in Baltimore and the State University of New York College of Medicine in Syracuse, N. Y.; on the faculty of the Bowman Gray School of Medicine of Wake Forest College in Winston-Salem, N. C., veteran of World War II; associated with the Danville Memorial and Winslow hospitals; died Dec. 14, aged 38.

Reed, William Wallace Ⓜ Topeka, Kan.; born in Mosinee, Wis., April 1, 1880; Kansas Medical College, Medical Department of Washburn College, Topeka, 1905; specialist certified by the American Board of Otolaryngology; served as president of the Shawnee County Medical Society; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served as state supervising ophthalmologist for the division of service for the blind of the Kansas State Board of Social Welfare; veteran of World War I; on the staffs of Stormont-Vail and St. Francis hospitals; died Dec. 22, aged 78.

Reynolds, Grover C. Ⓜ Brundidge, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; died Dec. 26, aged 74.

Rifici, Charles, Camden, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1929; served as physician for the Camden City Highway Department, physician for local board number 9 of Selective Service, city physician, and medical inspector of public schools; died in West Jersey Hospital Dec. 22, aged 56.

Riley, Philetus Holt Ⓜ Madison, N. J.; New York Medical College and Flower Hospital, New York City, 1937; certified by the National Board of Medical Examiners; on the staff of the Morristown Memorial Hospital, where he died Dec. 28, aged 53.

Scott, Kenneth Hazen Ⓜ Plainfield, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1942; veteran of World War II; on the staff of the Muhlenberg Hospital; died Dec. 25, aged 43.

Sher, David Daniel Ⓜ Miami Beach, Fla.; Boston University School of Medicine, 1934; certified by the National Board of Medical Examiners; veteran of World War II; formerly practiced in Marlboro, Mass., where he was on the staff of the Marlborough Hospital; died Dec. 12, aged 52.

Simons, Edwin J. Ⓜ Edina, Minn.; born in St. Paul June 23, 1896; University of Minnesota Medical School, Minneapolis, 1924; member of the American College of Chest Physicians; fellow of the American College of Physicians and International College of Surgeons; veteran of World War I; executive director of Minnesota Blue Shield (Minnesota Medical Services) and one of its founders; past-president of the Minnesota State Medical Association; a director of the Minnesota Public Health Association; received a distinguished alumni award in 1956 from the board of regents of the University of Minnesota; for many years practiced in Swanville, where he served as president of the First National Bank; served on the staff of St. Gabriel's Hospital in Little Falls; author of "Primary Carcinoma of the Lungs"; died Dec. 11, aged 62.

Slaney, Andrew F. Ⓜ Oconto, Wis.; Loyola University School of Medicine, Chicago, 1917; veteran of World War II; for many years city health officer; on the staff of the Oconto County and City Hospital, where he died Dec. 19, aged 66.

Stern, Robert Leo Ⓜ Beverly Hills, Calif.; Rush Medical College, Chicago, 1934; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World War II; deputy chief, hospital section, Los Angeles County Civil Defense Commission; on the attending staff, Cedars of Lebanon Hospital; on the staff of the Mount Sinai Hospital; past-president of the Beverly Hills Branch of the Los Angeles County Medical Association; died Dec. 17, aged 50.

Stevens, William Leary Ⓜ Shiloh, N. C.; University College of Medicine, Richmond, 1912; past-president of the First District Medical Society; served as health officer of Camden County; for 17 years medical advisor for the local board Selective Service; died in the North Carolina Memorial Hospital, Chapel Hill, Dec. 23, aged 70.

Stratton-Michener, Sina, Drexel Hill, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1895; served on the staff of the Pennsylvania Hospital in Philadelphia; died in Yeadon Dec. 16, aged 94.

Strother, Rodolph, Oberlin, La.; Memphis (Tenn.) Hospital Medical College, 1903; died Dec. 25, aged 76.

Tamraz, John Moorhaj Ⓜ Colonel, U. S. Army, retired, Miami, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1917; entered the regular Army in 1920; retired May 31, 1949; veteran of World War I; during World War II was chief surgeon in the China-Burma-India Theater and received the Legion of Merit for exceptionally meritorious conduct in the performance of outstanding service; fellow of the American College of Surgeons; died near Richmond, Ga., Dec. 8, aged 69.

Tan, Gilbert Wai Man, Sacramento, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1957; city schools physician; interned at the Sacramento County Hospital, where he served a residency, and where he died Dec. 5, aged 31.

Taylor, Jackson Phyromn Ⓜ Los Angeles; Meharry Medical College, Nashville, Tenn., 1922; on the staff of the Temple Hospital; treasurer of the Broadway Federal Savings and Loan Association; died Dec. 28, aged 61.

Townsend, Robert Glenn Ⓜ Grayson, Ky.; Tulane University of Louisiana School of Medicine, New Orleans, 1927; member of the American Academy of General Practice; for many years associated with the Stovall Memorial Hospital, where he died Dec. 20, aged 55.

Twohey, Joseph Thomas Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1932; member of the American Academy of General Practice; on the staff of St. Anne's Hospital; veteran of World War II; died Dec. 27, aged 51.

Van Zant, William Emory, Mandeville, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1901; died in St. Tammany Parish Hospital, Covington, Dec. 19, aged 81.

Vastine, Mary Frances Ⓜ Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1934; associate professor of radiology at her alma mater; certified by the National Board of Medical Examiners; specialist certified by the American Board of Radiology and the American Board of Otolaryngology; member of the Radiological Society of North America and the American College of Radiology; on the staff of the Hospital of the Woman's Medical College of Pennsylvania; died Dec. 11, aged 52.

Wasson, Valentina Pavlovna Ⓜ New York City; L. R. C. P., London and M. R. C. S., England, 1928; author of "The Chosen Baby" and co-author of "Mushrooms, Russia and History," written in collaboration with her husband, R. Gordon Wasson; attending pediatrician at New York Infirmary; died Dec. 31, aged 57.

Webb, Carol Castor Ⓜ Pensacola, Fla.; born in Albany, Ohio, March 31, 1895; Ohio State University College of Medicine, Columbus, 1918; honorary fellow of the Southeastern Surgical Congress; fellow of the American College of Surgeons; past-president of the Escambia County Medical Society; past-vice-president of the Frisco Railroad Medical Association; became local and later division surgeon of the Frisco Railroad and at the time of his retirement after 25 years' service was one of its consulting surgeons; veteran of World War I; in 1934 elected a director of the First Bank and Trust Company and served up to the time of his retirement; on the honorary staff of the Sacred Heart, Baptist, and Escambia General hospitals; past-president of the Kiwanis Club; died Dec. 29, aged 63.

Weber, Robert Cecil, Muncie, Ind.; Indiana University School of Medicine, Indianapolis, 1942; staff physician at the Veterans Administration Hospital in Marion, where he died Nov. 30, aged 40.

Wentz, John Wesley Ⓜ Pataskala, Ohio; Starling–Ohio Medical College, Columbus, 1910; for many years president of the school board; served on the staffs of the St. Ann's, Mercy, and St. Anthony hospitals, and the Grant Hospital, where he died Dec. 31, aged 73.

White, William Allen Jr. Ⓜ Boston; Harvard Medical School, Boston, 1921; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; assistant professor of clinical surgery at the Boston university School of Medicine; member and president of the staff of the Boston City Hospital; on the staffs of Faulkner Hospital, and New England Hospital; died in Milton Dec. 28, aged 62.

Williams, John Franklin Ⓜ Marion, Va.; Medical College of Virginia, Richmond, 1942; on the staff of the Southwestern State Hospital; died in the Lee Memorial Hospital Dec. 25, aged 58.

Williams, Percy Herbert Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1901; fellow of the American College of Surgeons; served overseas during World War I; for many years associated with the Lenox Hill and Lincoln hospitals; died Dec. 31, aged 83.

Willson, Harry Leigh Ⓜ Idaho Falls, Idaho; University of Pennsylvania School of Medicine, Philadelphia, 1914; past-president of the Idaho Falls District Medical Society; associated with the Idaho Falls Latter-Day Saints' Hospital and the Sacred Heart Hospital; served as president of the Idaho Falls Rotary Club; died Dec. 29, aged 69.

Wood, T. Kenneth, Williamsport, Pa.; Medico-Chirurgical College of Philadelphia, 1903; for many years practiced in Muncy, where he was one of the founders of the Muncy Valley Hospital, where for many years he was president; established the Muncy Historical Society and was its first president; served as editor of the society's historical journal, *Now and Then;* died Dec. 28, aged 81.

Wright, Harrison Garner Ⓜ Bellingham, Wash.; Johns Hopkins University School of Medicine, Baltimore, 1919; served as president of the King County Medical Society; first president of the King County Physicians Service; fellow of the American College of Surgeons; associated with St. Joseph's and St. Luke's hospitals; died Dec. 23, aged 68.

Yankoff, Peter Demetroff, Fort Smith, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1918; died Dec. 25, aged 74.

Young, Samuel Alexander Ⓜ Cleveland; Western Reserve University Medical Department, Cleveland, 1904; past-president of the Southeast Kiwanis Club; on the staff of St. Alexis Hospital, where he died Dec. 30, aged 79.

FOREIGN LETTERS

GERMANY

Federal Drug Act.—The draft of the Federal Drugs and Pharmaceutical Preparations Act was passed by the government of the Federal Republic of Germany. Although the manufacture of pharmaceutical products has increased steadily since the beginning of this century, German law has not provided for any official licensing of pharmaceutical manufacturers. There were also no legal provisions regarding the qualifications of a head of a pharmaceutical manufacturing plant, and no regulations prescribing equipment, working conditions, safety measures, or hygienic control of the workshops. There is, therefore, an urgent need for laws to safeguard the quality of pharmaceutical preparations and the manufacturing process. The new act bans the manufacture and sale of drugs which are injurious to health or which are spoilt or adulterated in any way. This ban also applies to drugs with misleading designations and drugs made up in a manner which may give rise to misinterpretation or misrepresentation. It also prescribes the labeling and description of pharmaceutical products; for example, the mode of application must be given and the active constituents must be stated, using the designations given in the German Pharmacopeia.

The same regulations apply equally to drugs of foreign manufacture. Any application for permission to manufacture pharmaceuticals will be turned down by the authorities concerned if the person in charge of the manufacturing plant is not suitably qualified. Permission will also not be granted if suitable rooms and equipment for the manufacture, testing, and storage of the products are not provided. The head of a pharmaceutical manufacturing plant must have completed his university training as a pharmacist, chemist, physician, dentist, or veterinarian, and must have had at least one year's practical experience in the manufacture of pharmaceuticals.

Special regulations govern the manufacture of serums and vaccines. The following data must be filed with the application for the registration of any products: qualitative and quantitative composition, fields of application with contraindications, form and mode of application, instructions for use, and results of pharmacological tests and trials if the components include substances whose effectiveness is as yet unknown. This registration merely serves to keep a check on the traffic in pharmaceutical products. The question of the actual need for any particular product is not considered; neither is its therapeutic efficacy tested. Judgment on the efficacy of and on the need for a certain product can only be passed after long and careful examination and thorough clinical trials. Such tests and trials by the government would lead to undue delays in registration which might not be in the interests of the patients or the manufacturer. Registration is to be refused if it is evident that the manufacture of the drug would violate the ban on spoilt or adulterated drugs, on drugs made up in a misleading manner, and on products not properly designated and described.

Kallikrein.—On the basis of his experiments on rats, M. M. Forell of Munich concluded that pancreatic kallikrein participates to a great extent in the digestive process. It is secreted with the pancreatic juice into the duodenum and either increases the absorption of foodstuffs by augmenting the blood supply of the intestinal vessels, or has a physiological effect due to its stimulating action on the intestinal contractions during digestion. It was also shown that the formation of kallikrein by the pancreas and the production of the other enzymes depend on the diet. A meat diet increased the formation both of ferments and of the circulatory hormone, while a diet rich in fat caused a reduction in ferments and production of the circulatory hormone. Reduced or absent urinary excretion of kallikrein followed blockage of the pancreatic ducts, but in diabetes produced by alloxan, despite extensive destruction of islet cells, the formation of kallikrein was undiminished. An incretory formation of kallikrein could not therefore be assumed.

In the urine of healthy persons kallikrein is present in an active form. Since patients with renal hypertension and adrenocortical hypofunction excrete little or no kallikrein, E. Werle and R. Vogel of Munich concluded that in these patients kallikrein would be excreted in the form of the pharmacologically ineffective kallikreinogen. By the action of trypsin on the urine they demonstrated that the urine of patients suffering from renal diseases contained kallikreinogen. The amount of kallikreinogen in the urine was always in direct proportion to the amount of protein. This indicated a passage of the renal barrier together with the plasma protein. The kallikrein released behaved chemically like pancreatic kallikrein: it was destroyed by boiling and inactivated by soy bean inhibitor and ovomucoid. Protein-free urines might,

The items in these letters are contributed by regular correspondents in the various foreign countries.

however, also contain kallikreinogen, as was demonstrated in patients with myeloid leukemia and diabetes. Kallikreinogen was not demonstrable in the urine of healthy persons.

F. Hollwich and A. Wethmar of Frankfort tested the influence of commercially prepared kallikrein on healthy retinal vessels by direct measurement in 80 persons with normal circulation. Kallikrein was administered in active form (20 to 40 units of Padutin), in depot form (40 to 100 units of Depot-Padutin), and in inactivated form in doses of 100 units. The inactivated form was a combination of Padutin with its natural inactivator and in this form it constitutes a depot that can be activated to 95% in the body by slight shifts in pH. After the intravenous injection of Padutin a measurable effect was observed in 15 to 30 minutes. The maximal effect was seen after 60 to 90 minutes; 20 units of Padutin increased the diameter of the arteries by about 8%, while with 40 units the increase was about 12%. The effect lasted three or four hours with the smaller dose and five or six hours with the larger dose. Corresponding to the protracted absorption of kallikrein from the Depot-Padutin, a dilatation of the retinal vessels occurred only after 45 to 60 minutes and maximal dilatation only after 3 hours. The duration of action with 40 units was 6 to 8 hours and with 100 units 10 to 13 hours. The lumen of arteries dilated by 9 and 11% respectively.

A dilatation of the vessels after three or four minutes of 14 to 21% lasting for about eight hours set in after slow intravenous injection of 100 units of inactivated kallikrein. This rapid and long-lasting effect was manifested by the fact that in the combination of Padutin and an inactivator about 5% of the substance was already present in active form, and that the remaining 95% was gradually activated. After intramuscular injection of inactivated kallikrein the effect set in after 30 to 45 minutes, but it was not inferior to the intravenous administration as regards duration and intensity. Comparative examinations with other vasoactive substances revealed that the effect of all forms of kallikrein application set in later, but (with equal or almost equally high maximum values) showed exceptionally long-lasting effects. This demonstration of the vasodilatory effect of kallikrein was in line with the numerous clinical observations on the therapeutic value of Padutin and Depot-Padutin as seen in circulatory disorders of the arteries of the retina due to spasm or thickening of the wall, in disturbed blood supply of the optic nerves, in senile macular degeneration, and in myopic macular degeneration.

The effect of kallikrein on the peripheral blood supply, which so far was almost exclusively tested on the vessels of the skin in man, was also examined on the musculature by G. Golenhofen and H. Hensel of Marburg. With their new methods, which permitted separate determination of the blood supply of the muscles and the skin, they observed that, through intravenous administration of 10 units of Padutin and 100 units of inactivated kallikrein, an increased blood supply of the muscles was effected in practically all patients. With Padutin this was sometimes about 100% and with inactivated kallikrein up to 200% of the values obtained when resting. An increased blood supply of the skin of the extremities was not seen with the two substances. Only the facial skin showed an increased blood supply and was reddened, with Padutin more than with inactivated kallikrein. The effect which in all cases subsided within a few minutes after a single injection was markedly longer with inactivated kallikrein than with Padutin. Measurement of blood pressure revealed a fall of the average pressure by about 15% for a maximum period of three minutes. At the same time the increase in the pulse rate was 40% on the average and lasted four or five minutes.

Intra-arterial recording of the blood pressure showed that the increased blood supply caused by Padutin was due to a genuine vasodilatation and not to an enhanced pressure-passive supply, but the rise in pulse rate must also be interpreted as a sign of an increased blood supply due to vasodilatation. The trials were carried out on 22 young, healthy persons in 111 single tests, and care was taken that the same room temperature was maintained in all tests and that the patients were in a relaxed position. As the drugs to be tested were slowly infused intravenously in physiological saline solution outside the field of vision of the persons, any possible psychic influencing factor was excluded. During the trial the blood supply of the muscles of the calves and forearm was recorded with the aid of a heat-conducting probe. The blood supply of the skin was measured with a heat-conducting measuring instrument on the ball of the thumb, the sole, or the cheeks.

INDIA

Adrenal Cortical Hypofunction and Amebiasis.—Kasliwal and Mathur (*Journal of the Indian Medical Association*, vol. 31, Dec. 16, 1958) observed that in some patients with chronic amebiasis such clinical features of chronic adrenal insufficiency as asthenia, hyperpigmentation of the skin and mucous membranes, hypotension, and loss of weight were present. They therefore performed tests to assess adrenal cortical function in such patients to find out whether they had adrenal cortical hypofunction. Nine patients with chronic amebiasis diagnosed clinically and by the presence of Entameba histolytica in the stools were thus studied. Cysts of E. histolytica were found in six, trophozoites in one, and two had cysts of both E. histolytica and Entameba coli. All of them had some clinical evi-

dence of chronic adrenal cortical insufficiency such as hyperpigmentation and asthenia. Healthy adults on whom the same tests were made served as controls. The age of these patients varied between 17 and 45 years, and the duration of illness between three months and nine years. The systolic blood pressure ranged between 80 and 104 mm. Hg and the diastolic pressure between 58 and 70 mm. Hg.

All showed hyperpigmentation of the skin and four had hyperpigmentation of the skin and mucous membranes. Two had marked asthenia and four had anemia. Hypoproteinemia and edema were present in all. One patient had hypochlorhydria, another achlorhydria, and one who had a pain resembling duodenal ulcer showed isochlorhydria. Three patients had such mental symptoms as inability to concentrate, insomnia, and marked fatigability. Three had such symptoms of hypogonadism as loss of libido and impotence in men and amenorrhea in women. Low values for serum sodium were obtained in eight patients and high values for serum potassium were obtained in seven. Mild absolute eosinophilia was present in two patients four hours after injection of 0.3 ml. of epinephrine; the eosinophil count fell by more than 50% in three patients and the percentage reduction in the other six was between 28.5 and 40. The urinary 17-ketosteroids ranged between 4.4 and 11.4 mg. in 24 hours in men and 3.1 and 4.7 mg. in women. Seven had a low urinary excretion of 17-ketosteroids and in two it was within normal limits. All these patients improved clinically after antiamebic and symptomatic treatment without any specific therapy for adrenal insufficiency. The exact cause for such insufficiency is not known, but chronic stress imposed by the various manifestations of chronic amebiasis or associated liver damage may be responsible.

Conference on Occupational Health.—Guide lines for the development of the occupational health services in southeastern Asia, made necessary by the increased speed of industrialization, were laid down in the conclusions reached at a southeastern Asia conference in Calcutta. The conference, jointly sponsored by the World Health Organization and the International Labor Organization, recommended that occupational health services be paid for by the employers but the provision of community health services covering workers and their families should be a governmental responsibility. Until community health services are fully developed, occupational health services should provide a certain measure of preventive and curative service, the extent of this being determined by local needs and resources.

These services should cover nonoccupational as well as occupational diseases. Institutes of occupational health should be developed to provide service, research, training, and technical information. Use should also be made of professional organizations in the field of occupational health. The training of physicians in industrial medicine should be given to the medical undergraduate, the physician entering the industrial health field, and the physician desiring to specialize in this subject. The training of industrial nurses and other auxiliary personnel is urgently needed. Persons trained in first aid should be available in every industrial undertaking, and regular courses in first aid should be given by the industrial physician. In establishing occupational health services it is not possible to exclude either legislation or education. Teamwork is a prime necessity in dealing with occupational health problems.

Prostatic Hypertrophy.—B. B. Ohri and co-workers (*Journal of the Indian Medical Association*, vol. 31, Dec. 16, 1958) studied 100 consecutive cases of senile enlargement of the prostate. All were subjected to the Freyer's method of suprapubic prostatectomy. Most of them sought medical attention because of acute retention of urine and were first treated with an indwelling catheter. Those without retention or who had retention with overflow were not catheterized. The series was divided into those whose bladder infection was mild (23), moderate (54), and severe (23). All were given 500,000 units of penicillin and 1 Gm. of streptomycin except those with severe infection who received 2 nitrofurantoin tablets, three times a day for four days. Most of this group had infection with Proteus vulgaris and Pseudomonas aeruginosa. Of the whole series 73 had acute retention. Those with a blood urea above 50 mg. per 100 cc. or with severe infection were treated with an indwelling catheter. Those who had severe urethritis or gross infection of the bladder and those whose blood urea level remained high in spite of the indwelling catheter (26) were subjected to a two-stage operation; 42 suffered from malnutrition and poor general health. The time spent in draining their bladders by an indwelling catheter or suprapubic cystostomy was used to improve their general condition.

The wound after operation usually healed in about two weeks. A bougie (size 9 to 12) was passed through the urethra on the ninth postoperative day as a routine. This prevented the formation of strictures in all but one patient who had a stone in the bladder. All patients received antibiotics postoperatively and nitrofurantoin was given to those with severe infection with P. vulgaris or Ps. aeruginosa. On discharge 42 had mild infection and others were free of infection. Postoperative hemorrhage occurred in four and two of them died. Of the 26 who had a two-stage operation, 4 died, 2 of complications of blood transfusion. The average stay in hospital was 22.3 days. Vasectomy was not done routinely. Gross wound infection after operation occurred in five patients but was treated successfully with nitrofurantoin.

Tuberculous Meningitis in Women.—K. R. Sathe (*Journal of the Association of Medical Women in India*, vol. 46, November, 1958) reported that tuberculous meningitis, mainly a disease of children, is seen more frequently in women than in men. In a series of 27 women with tuberculous meningitis the age of the patients ranged between 12 and 40 years. The antecedent tuberculous lesions were in the lungs in 9, the abdomen in 5, the spine in 3, and in the remaining 10 no antecedent tuberculous lesion could be detected. This may have been due to the fact that these patients were moribund on admission. In five the disease was associated with pregnancy and in nine it manifested itself in the postpartum period. For this reason pregnant women with known tuberculous lesions should be under constant supervision as the occurrence of tuberculous meningitis in them could be prevented by the early use of specific drugs. In this series 15 died. This high mortality was due to the late stage of the disease at the time of admission. Of those who survived seven had relapses. This emphasizes the need for prolonged and skillful after care.

All the patients showed the characteristic changes in the spinal fluid. Greater reliance was placed on the depression in the glucose content than on the chlorides in the diagnosis. Recovery was not considered complete till the glucose level returned to normal. Acid-fast bacilli could be demonstrated in only one patient. Streptomycin was given in doses of 1 Gm. twice a day in the beginning, followed by 1 Gm. daily for one to two months, combined with PAS and isoniazid. Streptomycin was given intrathecally in the early cases but this practice was discontinued because of the pain it caused and the tendency to favor complications. Cortisone was used in only one patient, due to its prohibitive cost.

Hepatic Coma.—B. B. Bhatia and co-workers (*Journal of the Indian Medical Association*, vol. 31, Nov. 16, 1958) found that the number of patients with hepatic coma treated in the last five years was much larger than that treated in the previous five years. During this period, however, a larger number of patients with hepatic cirrhosis and infectious hepatitis applied for admission, and the percentage of hepatic coma associated with these conditions remained the same (about 5% in those patients with cirrhosis of liver and 4% in those with infectious hepatitis). The incidence of hepatic coma in patients with infectious hepatitis was a little higher in this series than in those reported by observers in other countries. This may have been due to delayed treatment and lack of rest in the beginning of the illness which is common here. The authors' series consisted of 58 patients (42 men and 16 women, in 5 of whom the coma was precipitated by pregnancy).

The most common exciting cause of coma in this series was intestinal hemorrhage and the authors recommended that in any patient with cirrhosis of the liver, at the onset of mental symptoms, the stools and vomitus be examined carefully for blood. Other exciting causes were acute infection, administration of ammonium chloride and acetazolamide, high protein diet, and pregnancy. The administration of acetazolamide for the relief of ascites precipitated the onset of coma in two patients. In the group with infectious hepatitis the major precipitating cause was pregnancy. All five pregnant patients were in the third trimester. The occurrence of infectious hepatitis in this period should be regarded as a serious complication. In one patient coma followed physical exhaustion.

Superadded acute infection precipitated coma in all patients with cholangiohepatitis. Treatment therefore consisted in avoidance of physical exertion and prescribing a high-protein diet, ammonium chloride, acetazolamide, urea, meperidine, morphine, and barbiturates. The diet should consist mainly of carbohydrates and proteins. Acute infections and hemorrhagic tendencies should be controlled. Between 1,000 and 1,500 ml. of 25% dextrose solution should be given intravenously every day and one capsule of tetracycline should be given hourly by mouth or in nasal feedings. About 75 Gm. of glutamic acid was given daily but its value was doubtful. The authors do not advocate a completely fat-free diet. The ideal diet for the patient is high in carbohydrate, with average protein and fat content. ACTH and cortisone are probably useful when the coma has supervened on an infectious hepatitis.

Chlorpromazine for Mental Disease.—N. N. Chatterji (*Journal of the Indian Medical Association*, vol. 31, Dec. 1, 1958) treated with chlorpromazine 137 patients who had schizophrenia, 65 who had manic-depressive psychosis, 35 who had obsessions or compulsions, 32 who had hysteria, 25 who had paranoia, 16 who had involutional melancholia, 12 epileptics with mental symptoms, 8 who had an anxiety state, 4 who had dementia, 4 drug addicts, and 4 who had periodic depression. The age of these patients ranged between 15 and 45 years. The usual dosage was 200 mg. daily in divided doses. A Rauwolfia preparation containing lucin-H was also given to those with paranoia, paranoid schizophrenia, and manic excitement. The duration of treatment varied from three to six months. Most patients tolerated the drug well. Toxic symptoms met with in some were severe constipation, diarrhea, jaundice, cutaneous rashes, paralysis agitans-like symptoms, giant urticaria with serous discharge from all the body openings, and fever.

The differential blood count in patients with fever showed neutropenia, eosinophilia, and relative lymphocytosis while the total leukocyte count

showed leukopenia. Those who received large doses for a long time suffered from lethargy, weakness, and fatigue. Patients with schizophrenia, manic-depressive psychosis, and involutional melancholia responded well to the drug. Among the schizophrenics the best results were obtained in those with the catatonic variety. The symptoms disappeared within three weeks, and there was no need to give them shock treatments. In paranoid schizophrenics, although no response was obtained with chlorpromazine alone, good results were seen when it was combined with lucin-H, some patients being completely cured and others being able to go back to their social and occupational life in spite of the persistence of minor delusions.

In the paranoiac group, nine were completely cured with this combination. Manic-depressive psychosis showed an excellent response to chlorpromazine. The response was better in the manic phase when it was used in combination with reserpine. The depressed phase of manic-depressive psychoses subsided quickly with chlorpromazine. Results were good in patients with involutional melancholia but not in those with senile dementia. The increased excitability after fits in epilepsy were controlled with chlorpromazine. Among the psychoneurotic group, good response was seen in some patients with hysteria (mutism, aphonia, and fits). Good results were seen in obsessional neurosis. In drug addiction, although none was cured, the withdrawal period was easier with the use of chlorpromazine. Good results were obtained in patients with anxiety neurosis.

UNITED KINGDOM

Hazards for Young Doctors.—The hazards and rewards of different professions were discussed before the Royal Commission on Doctors' and Dentists' Remuneration. British Medical Association representatives said the road before the future hospital consultant was longer and more uncertain than that for men of other callings. The young physician, having completed seven years' undergraduate training, must serve in a hospital for a year as a provisionally registered practitioner and for two years in the armed forces before he will be free to decide on the direction of his career. By then contemporaries in other walks of life would have advanced to a point from which definite career prospects were in sight. Although the training for all professions is longer now than it used to be Dr. S. Wand, chairman of the B. M. A. Council, reminded the Commission that young men in some other fields are able to earn money en route. Invited to compare the young physician and the young barrister Dr. D. P. Stevenson, the association's secretary, said that whether or not the young barrister succeeded was very much in his own hands, but the young doctor might be forced into another branch of the profession outside the hospital field not because he was incapable but because there were no vacancies.

Dr. Gregory Dead.—Dr. J. C. Gregory, chairman of the All-England Lawn Tennis Club, Wimbledon, and a former Davis Cup player, died in the dressing-room of the club on Jan. 10, just after he had finished a doubles match. He was 55 years of age and had been in practice for nearly 25 years. He first represented England in 1926 when, as a member of the Davis Cup team, he played against Spain and France. From 1949 to 1953 he was the non-playing captain of the British Davis Cup team. After giving up the captaincy of the British Davis Cup team Dr. Gregory became vice-chairman of the All-England Club, and was elected chairman in 1955.

Future of the Tuberculosis Service.—The changes which have taken place in the last few years in the field of tuberculosis are the subject of an editorial in the *British Medical Journal* of Jan. 31. Although many beds for pulmonary tuberculosis have been closed because of the more rapid turnover of patients, hospital work has not decreased proportionately. On the other hand, the work of chest clinics may have increased. Since more patients suffer from pulmonary diseases other than tuberculosis, the work is much less routine in character than formerly. Figures obtained from 18 chest clinics showed that in one winter month of 1958 only 22% of new patients were diagnosed as having respiratory tuberculosis while 30% had acute respiratory disease and 27% had chronic respiratory diseases other than tuberculosis.

The Joint Tuberculosis Council strongly endorsed the view that facilities for the management of tuberculosis should be widened to serve patients with other respiratory diseases. This has already been done in many areas. Chest clinics are well able to coordinate inpatient, outpatient, preventive, and social services in the interest of patients with chronic respiratory diseases. They are peculiarly well suited to handle the problems presented by chronic bronchitis and to diagnose and treat bronchial carcinoma.

Perineal Carriage of Staphylococci.—Dr. M. Ridley, lecturer in bacteriology, St. Thomas' Hospital, London (*British Medical Journal*, Jan. 31, 1959) said that the possibility that the perineal region might be a carrier site on which Staphylococcus pyogenes var. aureus could multiply had been suggested but no information was available on the proportion of the population who are perineal carriers, whether they can disperse the organisms into free air, or the relationship between nasal and perineal contamination or carriage. A survey of 50 men showed that

52% had no Staph. pyogenes var. aureus in the nose or on the skin, 26% had this organism in the nose, generally in large numbers, but that the perineal area yielded fewer than 30 colonies from the six sites (total of 300 sites) chosen for examination. A further 12% had much greater degrees of contamination of the perineal area and were heavy nasal carriers as well. The remaining 10% had an equal degree of contamination of the perineal area but no Staph. pyogenes var. aureus in the nose, or at most five colonies. Thus, sufficiently large numbers of Staph. pyogenes var. aureus can be isolated from the perineal area of 22% of men to class them as perineal carriers. Further investigations showed that this state may persist for months in about 14%, that it is not due to fecal contamination alone, that the organisms can multiply in or on the perineal skin, that they may be of a different bacteriophage type from those found in the nose or feces, and that they may be dispersed into free air when the subject exercises in a cubicle.

Cost of Running Hospitals.—The cost of maintaining a patient in a London teaching hospital has risen to an average of $93 a week. This is shown in returns for the year ended March 31, 1958, and published by the Ministry of Health. The comparable figure in provincial teaching hospitals was $90. In nonteaching hospitals of 1 to 50 beds it was $59 and in those of 101 to 300 beds, $66. The average weekly cost in other types of hospital was as follows: chronic disease hospital, $26.50; maternity, $65; mental illness, $18; mental deficiency, $17; tuberculosis, $47; and children's acute disease, $63. Comparisons must be made with caution because of changes in accounting methods introduced in April, 1957. The net inpatient cost per patient at different hospitals averaged as follows: London teaching, $217; provincial teaching, $147; nonteaching, 101 to 300 beds, $130; maternity, $101; children's acute disease, $133.

Reducing Hospital Infections.—The widespread use of antibiotics, lack of facilities for isolating infected patients, and shortage of staff were among the chief causes of hospital infections, according to the report of Lord Cohen's Committee on Staphylococcal Infections in Hospitals. Unfortunately, funds and equipment are not universally available to allow staffs to carry out all recommended precautions (*Lancet*, Jan. 24, 1959). Staphylococcic disease was a major hospital problem before the era of antibiotics. The miraculous effect on it of penicillin, in 1944, was followed within two or three years by the appearance of the first penicillin-resistant strains of staphylococci. Today the drug is useless for most hospital epidemics. The breeding of drug-resistant strains has tended to increase the virulence of the organism and consequently to produce more severe infections. The fact that these are all theoretically avoidable in epidemic form led to the suggestion that penicillin be voluntarily withheld for a trial period of two years.

Lord Cohen's committee suggested that antibiotics such as erythromycin be kept solely for the treatment of infections due to strains resistant to other antibiotics and, except in emergency, should be prescribed only by a senior staff member. Strict observance of aseptic methods, not the use of antibiotics, is now necessary for the elimination of this serious problem. The report recommends extensive regular sterilization of all bedding, ward curtains, and other hospital materials with the suggestion that cotton blankets are more suited to this than woolen ones. The isolation of patients and of staff infected with whitlows and other staphylococcic infections is of paramount importance.

Reply to Attacks on Medical Profession.—Having read a letter from Sir Walter F. Hannay in the *Daily Telegraph* in which he deplored the trade union attitude of the British Medical Association, Prof. Charles Wells replied by means of an open letter in the *Daily Telegraph* of Jan. 22. He emphasized that the B. M. A. has never advanced the idea that physicians should withdraw service from their patients. What the B. M. A. suggested was withdrawal from the National Health Service and the provision to patients of continued medical attention at their own expense, the less affected areas subsidizing the more severely affected areas pending solution of their differences with the Minister of Health. Most trade unions would regard this as major lunacy.

A Cheaper Health Service.—A cheaper alternative to the National Health Service is being worked out by the British Medical Association. It might save the country as much as $840,000,000. The annual cost of the Health Service now exceeds $1,960,000,000 per year. It increases yearly as prices, salaries, and wages rise. The Association's Amending Acts Committee has laid down a series of basic principles which should underlie the new plan. The first is a statement that the preservation of private practice is essential to the development of medicine in this country, and its extension would insure a saving in public funds. The new plan would be financed by the state, the patient, and insurance. Payment by the patient would give him a sense of responsibility. There would be free care for the medically indigent. At present family physicians are paid a fee of $2.52 a year for each patient on their lists up to a maximum of 3,500 with an addition of $1.68 for each patient between the numbers of 501 and 1,500, bringing the fee for these patients to $4.20. This method of payment would be discontinued. Doctors would be paid a fee for each service rendered.

Concerning the possibility of abuse Dr. A. V. Russell, chairman of the Amending Acts Committee, said that there was some over-attendance in the early days of the Australian service, but this had been stopped by the profession itself. The principle of payment on a tripartite basis would free the service from the risk of political interference and enable the responsibility for its administration to be vested in a body on which the three contributing parties could be represented. Other principles laid down by the committee were (1) freedom of the physician, under safeguards, to prescribe whatever medicines he thought best; (2) restoration of the personal patient-physician relationship; (3) academic and professional freedom; and (4) avoidance of operating the health service in watertight sectional compartments.

Before any scheme is finally approved the draft must be considered by several interested committees. Endorsement by the Association's annual representative meeting would be necessary before such a plan became Association policy. The extent to which the state, the patient, and insurance, respectively, would pay for the cheaper alternative to the NHS has not yet been worked out. The only certainty is that the patient would contribute more than he does today through National Insurance, but he would stand to gain as a taxpayer.

The British Medical Association.—The Council of the British Medical Association has been forced to review its balance sheet. It has found that the existing dues for each ordinary members of $17.60 per year is insufficient to balance the budget. The prewar rate was $5.90. The Council decided, against strong opposition, to recommend to the representative body in July that the dues for 1960 be raised to $26.45. The principal reasons for the increase are inflation, the increase in the cost of the production of the *British Medical Journal*, the additional cost of the annual clinical meeting, further developments in regional offices, and the cost of fighting the Association's battles. Some believe that such a large increase will induce some members not to renew their membership, or to deter others from joining. Some suggest a means test whereby doctors in some of the lower income groups would pay a reduced charge while those in the surtax group would be expected to pay more. Many members fail to appreciate what the Association has achieved for them in its efforts to improve the conditions of service.

Poliomyelitis Vaccination.—Of the 6,250,000 people aged 15 to 26 who become eligible in the autumn for vaccination against poliomyelitis only 250,000 have been injected, and 96,000 of these have received only one dose. Ministry of Health officials and local health officers are disappointed and puzzled by the lack of response. Special efforts, such as evening clinics and injections at place of work, have been made to reach these young people. Local health authorities are starting a renewed drive. More special clinics and sessions at places of work will be arranged, and posters will urge young people to take advantage of the scheme. The acceptance rate for children up to the age of 15 is mounting, but both it and the response from expectant mothers must be improved.

Lung Cancer and Tobacco.—The Feb. 7 issue of the *British Medical Journal* contains three articles on lung cancer and tobacco. One of these, by R. Doll and co-workers, shows a definite relationship between the death rate from lung cancer and the length of discarded cigarette butts. In spite of the well-known difficulties of international statistical comparisons they found a distinct relationship in 16 countries between the reported cigarette consumption in 1930 and deaths from lung cancer in the period 1952-1954. Striking exceptions were Japan and the United States, which had a relatively high cigarette consumption but a relatively low incidence of lung cancer. In the United States one explanation may lie in the larger cigarette butt that the smoker discards. A comparison of cigarette butts specially collected and measured in Britain with similar data recently reported from the United States gives an average length of 30.9 mm. in the latter country against 18.7 mm. in the former. Of the cigarette butts in the British sample 67% were less than 20 mm. in length, and only 2.5% were as long as 30 mm. In the American sample less than 10% were smoked down to 20 mm., and 50% were discarded with 30 mm. or more still unsmoked. Such a large national difference in habits might greatly influence the national exposure to any carcinogen in cigarette smoke.

An article by I. T. T. Higgins of the Pneumonoconiosis Research Unit of the Medical Research Council discussed the relationship between tobacco smoking, respiratory symptoms, and ventilatory capacity in a series of 734 men between the ages of 25 and 64 who were randomly selected from urban and rural populations. A questionnaire was used to record respiratory symptoms and smoking habits. A clear relationship between smoking and persistent cough and sputum was invariably found, and smokers also tended to record more chest illness, wheezing, breathlessness, and chronic bronchitis than nonsmokers. Nonsmokers had a higher mean maximum breathing capacity than smokers; the best estimate of the difference, allowing for the size of the various groups studied, being 9 liters a minute. There was, however, no significant downward trend with increasing tobacco consumption among the smokers.

CORRESPONDENCE

THERAPY IN THE ANEMIAS

To the Editor:—In the June 7, 1958, issue of THE JOURNAL, page 735, an article entitled "Current Status of Therapy in Anemias," by Lichtman, states that parenterally administered iron, for example, in the form of an iron-dextran complex (Imferon) in great excesses over a long period of time will produce "exogenous hemochromatosis." Since parenteral therapy with properly calculated dosage of iron-dextran complex should be discontinued when a hematological response has been obtained, as well as when this type of therapy fails or the patient eventually becomes anemic, iron-storage diseases, i. e., hemosiderosis or hemochromatosis, should not occur under these circumstances, because the possibility of iron overload is eliminated. The subject of iron-overload has been discussed in a textbook, "Iron in Clinical Medicine" (edited by Wallerstein and Mettier, Berkeley, University of California Press, 1958). The question of whether hemosiderosis progresses to hemochromatosis has been answered both affirmatively and negatively. Much of the difference of opinion is a result of the different clinicopathological criteria used in defining hemosiderosis, hemochromatosis, and cirrhosis. From the studies of Baggenstoss, Weir, Kark, and myself—based on autopsy data from 35 patients with primary hemochromatosis, 7 with secondary hemochromatosis, and 21 with hemosiderosis and data from 10 living patients (9 with primary hemochromatosis, and 1 with secondary hemochromatosis)—we were able to establish definite clinical and pathological criteria mandatory in defining these conditions.

The evidence that iron per se does not produce hemochromatosis is summarized as follows: 1. The administration of iron, intravenously, orally, or in the form of blood transfusions in human beings, causes transfusional hemosiderosis but not hemochromatosis. 2. The administration of iron, orally or parenterally or in combination with cirrhotogenic diets, over long periods to experimental animals produces only hemosiderosis. 3. The amount of iron administered to patients through blood transfusions does not correlate with the degree of cirrhosis or hepatic, myocardial, or pancreatic fibrosis. 4. Oral Fe^{59} absorption studies, serial liver biopsies, serum iron and iron-binding capacity determinations, and evaluation of genetic traits of patients with hemochromatosis differ from those with hemosiderosis, which is actually only a pathological condition.

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ACROMIOCLAVICULAR SEPARATIONS AND DISCUSSIONS OF PAPERS

To the Editor:—The report on suspension cast for acromioclavicular separations and clavicular fractures, published in THE JOURNAL (**169**:672-675 [Feb. 14] 1959) and presented at the A. M. A. meeting in San Francisco last June, leaves much to be desired. The paper gives the impression that many patients have been treated this way and that the results were good. However, what we saw when the paper was given was most inconclusive. It appeared that the acromioclavicular joints were still separated in the cases shown and that the suspension cast gave no better results than did a posterior figure-of-eight support in bilateral clavicular fractures. It is unfortunate that the discussion of this paper was not also presented in THE JOURNAL. In it these points were clearly brought out and doubt was cast on the value of this method of treatment. Many papers published in various journals lose their value when the discussion at the time of presentation is not also reproduced. Frequently the discussion points up the good and bad points of the method presented and entirely changes one's concept of whether or not it is worthy of a trial.

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F. B. I. ITEMS IN THE JOURNAL

To the Editor:—In THE JOURNAL (**169**:640 [Feb. 7] 1959) is a letter from Dr. Guttmacher, of Baltimore, in which he criticizes the occasional acts of cooperation of THE JOURNAL with the F. B. I. I hope that there will be a continuation of appropriate aid to our law enforcement officers. I am sure that most physicians in the United States feel the same way.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Malpractice: Breach of Warranty.—This was an action for damages against the defendant psychiatrist. From a summary judgment for the defendant in the trial court, the plaintiff appealed to the United States court of appeals for the District of Columbia.

Because of the plaintiff's condition, the defendant recommended the administration of a series of electric shock treatments. Prior to giving them, contended the plaintiff, the defendant advised that the treatments were "perfectly safe," and she said she submitted to the treatments in reliance on such assurance. When she regained consciousness after one of the treatments, the plaintiff found that she had a fractured left arm.

The defendant denied making the statement attributed to him by the plaintiff. In a deposition, however, he said that the plaintiff's fracture was caused by the convulsive seizure which ensued as a result of the electric shock treatment and that in his practice this had occurred on seven or eight other occasions.

Doubtless, said the court, a physician's statement that he would cure a disease could seldom if ever be regarded as a warranty. But that is not this case. The statement attributed to the defendant, that shock treatments are "perfectly safe," contains less of prediction and more of present fact. We think this statement, if the defendant made it and did not qualify it in any way, might properly be found to be a warranty.

The summary judgment in favor of the defendant was therefore reversed. *Johnston v. Rodis*, 251 F (2) 917 (1958).

Malpractice: Delay in Using Lipiodol Dye X-Ray Technique with Lipiodol.—This was an action for damages for pain and suffering caused by the alleged negligence of the defendant surgeon. From a judgment for the defendant, the plaintiff appealed to the court of appeals of Maryland.

The patient, deceased wife of the plaintiff, was suffering from an advanced stage of cancer of the descending colon when she was referred by her own physician to the defendant for surgery. He found that a large cancer in the upper part of the descending colon had gone through all three coats of the intestine and had become attached to the back. He felt that complete removal of the tumorous mass would afford the best chance of preventing the spread of the cancer and of survival of the patient. In spite of the difficulty he removed a large portion of the colon, together with the large tumor, all in one piece and then joined together the two remaining sections of the intestine. After the operation the patient continued to have a fever for six weeks for which a variety of treatments were used including drugs, blood transfusions, and drainage operations. After the second drainage operation consultants were called in to attempt to locate the continuing difficulty. The consultants concluded "that there was still a collection of pus somewhere in the abdominal cavity that required drainage." It was suggested that two types of x-rays be taken, chest x-rays to determine the level of the diaphragm, and instillation of lipiodol dye to determine whether or not there was a tract that led to a pus pocket. The suggestion of injecting the dye in the fistulous area was adopted, the tract where the pus had accumulated showed up clearly, and an effective drainage operation was performed.

The gravamen of the plaintiff's charge was that the defendant delayed unduly in the use of the dye technique to locate accurately the pus accumulations.

There is a presumption, said the court, that a doctor has performed his medical duties with the requisite care and skill. The burden of proof is on the plaintiff to show both a lack of the requisite skill or care on the part of the doctor and that such want of skill and care was a direct cause of the injury; and if proof of either of these elements is wanting the case is not a proper one for submission to the jury. The plaintiff's main difficulty was the lack of affirmative proof of negligence on the part of the defendant.

We think, concluded the court, that the plaintiff has failed to meet the burden of presenting evidence which would support a finding of negligence. Though it might be inferred that if he had used lipiodol dye sooner the patient would have fared better, we do not think that the plaintiff has produced proof that the defendant was guilty of negligence in failing to use it sooner and in seeking to locate and drain the pus pockets by other means. He was clearly successful in locating a pus pocket on his first drainage incision, and that fact alone seems to prevent an inference that a dye injection was a necessary means of discovering the location of pus. Nor do we think that there is any such common knowledge of the use and efficacy of the dye method as to warrant us in holding that the jury might find, without supporting expert testimony, that the surgeon was wanting in reasonable diligence, skill, and learning because he failed to use this dye test in addition to others at an earlier stage of postoperative care of the patient.

Accordingly the judgment of the trial court in favor of the defendant physician was affirmed. *Lane v. Calvert*, 138 A (2) 902 (Md., 1958).

MISCELLANY

FOREIGN MEDICAL GRADUATES

A PROGRESS REPORT

T. Stewart Hamilton, Hartford, Conn.

The number of graduates of foreign medical schools taking the examination of the Educational Council for Foreign Medical Graduates is increasing by almost geometric progression and will reach an expected peak in 1959. In March, 1958, 298 physicians wrote the first examination; 844 wrote the September, 1958, examination; and some 2,300 have applied for February, 1959. It is important that we assess the status and the potential of this program as we plan for the future.

The ECFMG was formally established in 1957, after preliminary discussion and planning over the previous decade.[1] Its primary objective was to promote opportunities in the United States for advanced studies in medicine, to the end that the level of medical care might be raised throughout the world. Its primary concern was to safeguard the health care and welfare of the American public; therefore, it sought to determine that foreign medical graduates participating in patient-care educational programs in the United States had reached a level of educational attainment comparable to that of graduates of medical schools in the United States and Canada. ECFMG is sponsored by the American Medical Association, American Hospital Association, Association of American Medical Colleges, and Federation of State Medical Boards of the United States. Its trustees, composed of representatives of the sponsoring organizations and the public, have developed and implemented a plan for evaluation of credentials and administration of a qualifying examination. At the same time they have sought and obtained funds from the Kellogg and Rockefeller Foundations to initiate the program and engaged Dr. Dean F. Smiley as the executive director.

In March, 1958, the first examination was given to 298 physicians in centers in the United States and Canada. These graduates of foreign medical schools had already had from 1 to more than 20 years' experience with medicine in the United States. Questions were taken from those tested and used by the National Board of Medical Examiners. The questions were selected as being least likely to confuse those whose command of English was somewhat limited. Of these 298 physicians only 151 (51%) attained a passing grade of 75 or higher,[2] a disappointing result.

Director of the Hartford Hospital.

At the American Hospital Association convention in September concern was expressed that the new examination would greatly reduce the numbers of interns coming to the United States. Concern was also expressed that agreement by the National Intern Matching Program to accept certified foreign medical graduates for matching along with graduates of United States and Canadian schools would further deplete the intern supply available to hospitals now relying on these men and women to fill their quotas. These questions were voiced both at the Council on Professional Practice Review Committee meeting on Aug. 17, 1958, and later before the House of Delegates. Although no formal action was taken, the record of these proceedings included the suggestion of one delegate that "(a) The American Hospital Association . . . take steps to defer if at all possible, the inclusion of foreign medical graduates into the intern matching program until the program has been further evaluated and (b) to examine and test the present mechanism in view of the high percentage of failures."[2]

This seemed to relieve the administrators' minds, at least for the moment, since a program on the subject of the foreign medical graduate held later in the convention attracted a relatively small audience and evoked few comments or criticisms. It seemed that most delegates, while worrying about the possible implications of the program for their own institutions, recognized the need for such a controlled plan.

The ECFMG Examinations Committee reviewed the results of the March examination with great care and, noting that many who took it complained of its length, recommended that the number of questions be reduced and the time for its completion be extended. The question of lowering the passing grade from 75 to 70 was discussed at length. Decision against such a step was made on the ground that if it were taken the ECFMG could no longer state that the certified physician had reached a level of educational attainment comparable with that of a graduate of a United States school.

Dr. John P. Hubbard toured the world for the ECFMG during the summer of 1958 and set up 27 examination stations in Central and South America and overseas. On Sept. 23, 1958, 844 graduates of foreign medical schools whose credentials had been studied and approved wrote the new examinations, 707 in the United States and Canada and 137 in foreign centers.[3] Of those writing in U. S. stations 52.4% passed, which indicates that changing the examinations to reduce the number of questions and extend the time for their completion had little if any effect, for 51% had passed the first examination. A new and serious problem arose when the scores of those writing the examination overseas were compared with those of United States examinees. This is demonstrated graphically in the chart. While those writing in the United States did

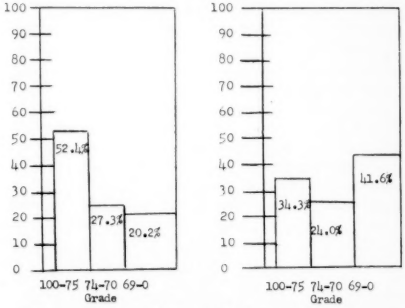
rather better than the March examinees, scarcely more than one-third of those writing in foreign stations attained a passing grade.

It was at once obvious to the Examinations Committee that to limit the number of certified foreign medical graduates from without the United States and Canada to barely more than one-third of those taking the examination would be serious indeed. It was obvious as well that, in comparing the results of the two groups, students benefited greatly from what they learned in the United States. For these reasons it was decided that a new category be established, called Temporary Certification. Temporary certificates, valid for two years' postgraduate training in the United States, will be given to examinees who attain scores of 70-75. By the end of the two years the graduate will be expected to have written and passed the certifying examination. The new category of Temporary Certification will entitle the holder to apply for any approved internship in the United States and to be matched through the National Intern Matching Program.

The decision to issue temporary certificates to those whose scores were within five percentage points of a passing grade was approved by the trustees as an expedient measure in the face of the unexpectedly poor showing of those who wrote the examination outside the United States. By its issue the percentage of examinees receiving either permanent or temporary certification was raised to 76.2. Of those writing in the United States 79.7% attained grades of 70 or higher while of those writing in foreign centers 58.3% attained such scores. Of the 844 who wrote the September examination 226 (26.7%) will receive temporary certificates. If they plan to take more than two years' postgraduate training in the United States it will be necessary for them to retake and pass the ECFMG examinations during that period. The two years is deemed necessary to give the graduate time to improve his knowledge, reapply, and rewrite the examination.

What of future examinations? As noted above, 2,300 graduates of foreign medical schools have applied to write in February, 1959; it is expected that at least an equal number will apply for the September, 1959, and February, 1960, examinations. After July 1, 1960, the date when all graduates holding internship and residency appointments will be expected to have qualified, the number of applicants should fall to between 2,000 and 3,000 per year. These will be graduates of foreign medical schools who are seeking appointments for the first time together with those holding temporary certification and others who apply to rewrite the examination. Examinations will be given as at present both in the United States and in foreign stations. Cost of the administration will be borne by both the applicants and the hospitals appointing them, the charge being $50 to the applicant and $75 to the hospital. Those eligible to apply will be graduates (and in some instances students in their last year) of schools listed in the World Health Organization World Directory of Medical Schools. Applications will be screened at the Council's headquarters, 1710 Orrington Ave., Evanston, Ill. Although actual scores and results of examinees by school or by nationality will be kept confidential lists of those certified will be made available to state medical boards and other authorized bodies.

While the program is scarcely under way and has had to face the usual problems of any new organization it already shows promise of the accomplishment of its twofold purpose: improving educational opportunities for graduates of foreign medical schools and insuring an adequate quality of care for patients. State boards of medical examiners in 16 states, for example, have already agreed to accept ECFMG permanent certificates as evidence for admission of a foreign-trained physician to their licensing examinations. It is expected that ECFMG permanent certificates will soon come to be regarded around the world as evidence that the holder has attained a level of medical competence equivalent to that of a graduate of a United States or Canadian school. In order to succeed the ECFMG will need the continued support of its sponsoring agencies and their membership. If it succeeds it can be a vital factor in the improvement of world medicine and world health.



Results of examinations taken by graduates of foreign medical schools at United States stations (*left*) and at foreign stations (*right*).

This article is being published simultaneously in the April 1, 1959, issue of *Hospitals*.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Serum Triglycerides in Coronary Artery Disease. M. J. Albrink and E. B. Man. A. M. A. Arch. Int. Med. **103**:4-8 (Jan.) 1959 [Chicago].

Lipids are transported in serum as constituents of 3 major classes of compounds: cholesterol and its esters, phospholipids, and triglycerides or neutral fat. Most investigations in recent years have centered about the notion that serum cholesterol plays a causative role in the development of coronary artery disease. Although triglycerides rather than cholesterol are chiefly responsible for turbidity of serum and constitute an important fraction of β-lipoproteins, the quantitative estimation of triglycerides has been largely neglected in studies of serum lipids in coronary artery disease. The present research was undertaken to observe the interrelation of the 3 major serum lipid fractions. The subjects were 100 patients with a history of myocardial infarction. The group included 82 men and 18 women, ranging in age from 21 to 78 years, the greatest number being in their 50's. Control subjects included healthy medical students, industrial workers, and hospital patients without vascular disease and without known metabolic disorders.

Elevations of serum triglycerides above 5.5 mEq. per liter (about 160 mg. per 100 cc.) occurred in only 5% of normal young adults, in at most 30% of normal men over 50, and, if the effects of acute illness were excluded, in 85 to 90% of patients with coronary artery disease. The authors believe that few, if any, other lipid measurements which have been reported effect such a clear-cut separation between normal and coronary subjects. The observations reported suggest that an error in the metabolism of triglycerides is the lipid abnormality operative in coronary artery disease. It may be that other findings commonly reported in this disease, such as increased cholesterol, increased low-density lipoproteins rich in triglycerides, and prolonged and intensified alimentary lipemia, are secondary to decreased efficiency of triglyceride utilization with resulting accumulation of triglycerides in plasma. It is tempting to speculate on the significance of these findings in relation to the energy metabolism of the heart, particularly in the light of recent evidence that fat is an important source of fuel for the normal myocardium, that triglycerides are turned over with great rapidity by heart tissue, and that lipoprotein lipase occurs in high concentration in myocardial tissue.

The Post-Myocardial-Infarction Syndrome: A Report of 44 Cases. W. Dressler. A. M. A. Arch Int. Med. **102**:28-42 (Jan.) 1959 [Chicago].

The author presents observations on 44 patients with recent myocardial infarction, whose clinical picture did not conform to the textbook pattern of myocardial infarction. There were prolonged and recurrent fever and chest pain. Relapses occurred frequently and caused prolongation of the clinical course by several weeks or months. Such features are usually attributed to recurrent myocardial or pulmonary infarction. However, in the patients studied, electrocardiographic signs of extension of myocardial infarction were absent, and there were no features indicative of phlebothrombosis in the lower extremities or obvious signs of pulmonary infarction. Instead, evidence of generalized pericarditis with effusion often associated with pleurisy and pneumonitis was observed. This triad, which closely resembles the postcommissurotomy syndrome and idiopathic pericarditis, has been referred to as the postmyocardial infarction syndrome. The 44 patients were observed at the Maimonides Hospital in Brooklyn, N. Y., in the course of the past 2 years.

Several illustrating case histories are presented, and the author discusses various aspects of the postmyocardial infarction syndrome. It differs from the common "pericarditis epistenocardica" by longer duration of fever and chest pain and by relapses of fever and pleuropericardial pain; the pericardial friction rub lasts longer or occurs later than usual; there is pericardial effusion which is often associated with pleurisy and pneumonitis; recurrences are common. The exudate may be hemorrhagic. The postmyocardial infarction syndrome is readily distinguished from the 2 conditions for which it has been mistaken: (1) from extension of myocardial infarction, by the pleuropericardial character of the pain and the absence of additional changes in the electrocardiogram, and (2) from pulmonary infarc-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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tion, by the finding of evidence of pericarditis. "Enlargement of the heart," which is often erroneously diagnosed on x-ray evidence, can be ruled out by serial x-ray studies which demonstrate rapid shrinking of the heart silhouette. It is estimated that the postmyocardial infarction syndrome complicates from 3 to 4% of the cases of myocardial infarction. Its etiology is unknown, but it is thought that sensitization by necrotic muscle tissue may be the responsible factor. The syndrome is benign, but relapses may occur repeatedly. Adrenal steroids promptly abolish fever and pain, but their use should be reserved for patients with severe intractable pain or with a prolonged course of illness. Anticoagulant therapy is dangerous. A case is reported in which the use of anticoagulants led to fatal cardiac tamponade.

Macroglobulinemia of Waldenstrøm: Brief Review with Description of Cases. J. O. Alvsaker. Tidsskr. norske laegefor. **78**:1171-1173 (Dec. 1) 1958 (In Norwegian) [Oslo].

Macroglobulinemia is a chronic condition with fatal outcome, which occurs in both sexes but especially in older men. The symptomatology is marked by vague general symptoms, such as asthenia, dyspnea, anorexia, and loss of weight. Often after several years there is a tendency to bleeding, with hemorrhagic manifestations localized to the skin, mucous membranes, retina, central nervous system, and gastrointestinal tract. Some patients show reduced resistance to infection, and intravascular hemolysis has been described. Clinical examination often reveals general lymph node inflammation and in some cases splenomegaly and hepatomegaly. The sedimentation reaction is greatly increased. On fractionated serum albumin determinations, hyperglobulinemia with inverted albumin-globulin index is found. Establishment of macroglobulins on ultracentrifugation is pathognomic. Macroglobulinemia may be accompanied by disturbances in the lipid metabolism with reduced cholesterol in the blood. The primary disturbance seems to be localized in the reticuloendothelial system. In a case of long-continued, greatly increased sedimentation reaction of unknown cause, and in vague hemorrhagic manifestations with increased sedimentation reaction, the blood picture and the electrophoresis diagram will direct attention to macroglobulinemia. While verification of the diagnosis depends on ultracentrifugation, simpler laboratory tests can make the diagnosis probable. Positive formolgel reaction in less than 10 minutes testifies for macroglobulinemia. In the case described, in a man aged 70 years, there was a typical picture of the disorder, early in the course, with marked hyperglobulinemia, characteristic electrophoresis diagram, and 28% macroglobulins seen on ultracentrifugation. The hematological picture was also characteristic, the formolgel reaction being strongly positive and the cholesterol value in the blood slightly reduced. The case is considered as primary macroglobulinemia.

Clinical Experience with the use of Neomycin in Hepatic Coma. W. W. Faloon and C. J. Fisher. A. M. A. Arch. Int. Med. **103**:43-53 (Jan.) 1959 [Chicago].

Of the many therapeutic regimens that have been employed in hepatic coma, the withdrawal of protein together with the oral administration of wide-spectrum antibiotics has reportedly given the most favorable results. Observations in the laboratory with which the authors are connected indicated the efficacy of orally administered neomycin in reducing blood ammonia concentrations even when protein feeding was continued. Therefore, they deliberately gave protein by mouth while neomycin was given. The major objective of this regimen was the reduction of ammonia formation by reducing the intestinal bacterial flora while attempting to maintain optimal nutrition. Twenty-two patients with alcoholic cirrhosis were followed during 25 episodes of coma or impending coma. This series included some patients who received acetazolamide (Diamox) or who had gastrointestinal hemorrhage. These might have been the chief factors responsible for precipitating hepatic coma. Since it is likely that such patients will always be found in any extensive series of hepatic coma patients, the authors report their observations on these patients as well as on those in whom neurological disorders developed spontaneously.

Improvement resulted in 23 of the 25 episodes of coma. Eleven of the 22 patients died, but in 9 of these 11 some improvement was noted before death. Eighteen patients received protein from the beginning of therapy with neomycin, and, of these, 7 lived and 11 died, but some improvement was noted before death in 9 of the latter. Four patients received no dietary protein, and all survived, but, of these, 3 had bleeding and thus had protein within the intestinal tract. A decrease in the level of blood ammonia was observed during therapy in 16 of the 18 patients in whom it was determined. Of those whose ammonia levels fell, 8 lived and 8 died, with all the patients showing some improvement prior to the final outcome. Death occurred in both patients in whom the ammonia level did not fall during neomycin therapy, and neither patient exhibited improvement. No significant difference in survival rate was observed between patients receiving more than 25 Gm. of protein and those receiving less than 25 Gm. An unfavorable prognosis in these patients was found to be associated with increasing depth of coma after therapy was initiated and with the presence of jaundice.

Remission of the Hematological and Clinical Symptoms in Acute Leukemia After Treatment with Prednisone and 6-Mercaptopurine. P. Longo. Policlinico (sez. prat.) **65**:1639-1648 (Oct. 27) 1958 (In Italian) [Rome].

Complete remission of the hematological and clinical symptoms was obtained by treating a 17-year-old youth with acute leukemia with prednisone and 6-mercaptopurine. The first symptoms of the disease occurred in the patient one year before admission to the hospital. Upon admission the patient received several 200-cc. transfusions of fresh whole blood and treatment with analeptic drugs and vitamins. Prednisone and 6-mercaptopurine were given 4 days later. Prednisone was administered first in a dose of 30 mg. per day and later in a dose of 80 mg. per day, which was continued for 22 days; 6-mercaptopurine was administered in a dose of 150 mg. every 24 hours, which was continued throughout the period the patient remained in the hospital and was reduced to 100 mg. per day after discharge from the hospital. Three additional 200-cc. blood transfusions were made before discharge from the hospital.

The condition of the patient was critical during the first 15 days he spent in the hospital. A gradual improvement could be observed after this period. The patient started to take some food, and the temperature tended to decrease. Later a marked improvement of the objective and subjective conditions followed day by day. Swelling of the lymph nodes became reduced and almost disappeared. The contour of the spleen and of the liver became normal. The infection of the mouth and throat healed, and no trace was left of it. The color of the patient became normal, and the body weight, which was 57.3 kg. (126 lb.) on admission, went up to 65 kg. (143 lb.). Fever disappeared completely 6 weeks after admission, at which time the appetite increased markedly and the digestive process was normal. The patient was discharged from the hospital after 16 weeks and, when seen 1 month later, was found to be in good general condition. The hematological examination at this time gave normal results.

Armchair Treatment with and Without Anticoagulants in Cardiac Infarction. S. Helander. Acta. med. scandinav. **162**:351-359 (no. 5) 1958 (In English) [Stockholm].

The author reports on 307 patients with cardiac infarction, who were admitted within 3 days of onset and received armchair treatment, with and without anticoagulants, at the Karolinska Sjukhuset in Stockholm between 1952 and 1956. The aim of the armchair treatment was to relieve the heart muscle. The patients were divided into 3 groups according to the severity of their condition. Group 3 included the mild cases; group 2 included patients with the usual clinical symptoms of cardiac infarction, with fever, raised erythrocyte sedimentation rate, and leukocytosis; and group 1 included the most severely ill patients, with additional manifestations of shock and a fall in blood pressure. Fifteen of the 307 patients died within 12 hours after admission and are not included. Of the remaining 292 patients, 112 were treated in an armchair and were given anticoagulants (10% of these died); 100 were treated in an armchair without anticoagulants (15% of these died); and 80 were treated with bed rest and anticoagulants (26% of these died). It is significant that 6% of the patients from group 2 who received armchair treatment with anticoagulants and 16% of the patients from the same group who received armchair treatment without anticoagulants died, whereas of the patients of group 2 who received treatment with anticoagulants and bed rest 22% died. Most of the patients who died showed ominous prognostic signs, such as arrhythmia in cardiac failure or heart block, and about half of them had had a previous attack of cardiac infarction, as postmortem examination had revealed. Of the patients treated in an armchair, there were 14 who had had a previous attack of infarction among the 25 patients who died. Twelve patients of the armchair group had a septal infarction, against 9 of 21 patients treated with bed rest. The frequency of embolic complications was negligible in all groups and could hardly have had any effect on the mortality.

An analysis of the immediate causes of death in cardiac infarction seems to suggest that armchair treatment lessens the burden placed on the heart muscle and diminishes the risk of occurrence of pulmonary edema. Embolic complications do not seem to have played any role in determining the difference in mortality rates between those treated with anticoagulants and those who did not receive anticoagulants. Armchair treatment seems to be a good prophylaxis against thromboembolic complications in patients with cardiac infarction.

Syndromes of Thyroid Hyperfunction in Old Age: Clinical Study. C. de Nogales Quevedo and M. Santaló Rovira. Med. Clín. **31**:83-105 (Aug.) 1958 (In Spanish) [Barcelona, Spain].

Three hundred patients with hyperthyroidism were observed at the hospital of the University of Barcelona; of these patients 20 (17 women and 3 men) were between the ages of 50 and 70 years. The older patients complained of repeated bouts of hyperthyroidism, with cardiac decompensation and periods of either nervousness or depression. Psychic trauma was the only, or the predominant, causal factor of hyperthyroidism in more than half of them. On hospitalization, all these patients reported considerable loss of weight during the past few months, and they all had tachycardia and

tremor. Hyperthyroidism was of either the apathetic (Lahey's) type or the type of exophthalmic goiter. Hyperthyroidism of the apathetic type had appeared in 10 women several years after the menopause. The cardiovascular disease was severe, 5 of the patients having atrial fibrillation with complete arrhythmia. Exophthalmos and goiter either were not present or were very mild. The constant psychic feature was depression. Hyperthroidism of the type of exophthalmic goiter appeared in 7 women immediately or shortly after the menopause. The ocular, thyroid, and cardiovascular symptoms were the same as those observed in patients whose exophthalmic goiter had developed at a younger age. The psychic feature was constant nervous tension.

The treatment of these older patients with hyperthyroidism consisted of the administration of methylthiouracil in daily doses which ranged from 0.15 to 0.3 Gm. This dosage was given in 3 or 4 fractional doses for several days during early therapy. Then the patients were placed on maintenance therapy in which the dosage was individually determined and was given for 3 or 4 months until complete remission was obtained (100% satisfactory results were reported in all these cases). Remission has lasted for several years since discontinuation of the treatment in all the patients but 2. These 2 patients had a recurrence 7 months and 1 year, respectively, after the first remission, but a second complete remission, which has lasted several months, was obtained once more from the administration of methylthiouracil. The authors conclude that thyrotoxic goiter in older patients is a clear indication for treatment with methylthiouracil; the drug is well tolerated. Surgical treatment of hyperthyroidism in this age group is indicated only in cases of nodular goiter or when canceration of the goiter is threatening. Seven representative cases are reported.

A Comparative Study of the Effect of Transfusion of Fresh and Preserved Whole Blood on Bleeding in Patients with Acute Leukemia. E. J. Freireich, P. J. Schmidt, M. A. Schneiderman and E. Frei. New England J. Med. **260**:6-11 (Jan. 1) 1959 [Boston].

Gross bleeding in patients with acute leukemia is closely related to thrombocytopenia. With the development of plastic and other nonwettable surfaces, the transfusion of viable platelets that circulate for 5 to 7 days was demonstrated, but because of difficulties involved in platelet transfusion, it cannot be employed as a standard therapeutic procedure. For these reasons, freshly drawn whole blood, collected over nonwettable surfaces, has been utilized for the treatment of thrombopenic bleeding in patients with acute leukemia. Preliminary clinical observations of the effect of fresh whole-blood transfusion on hemorrhage in acute leukemia indicated definite benefit in only an occasional patient. Moreover, the extreme irregularity of hemorrhage in these patients, as well as the frequently transient nature of the hemostatic effect, often made clinical judgement of effectiveness extremely difficult. In view of the extra time, effort, and expense involved in utilizing fresh blood for transfusion, it seemed necessary to evaluate quantitatively the effect of this treatment.

The present study was designed as a controlled, comparative blind study, with banked whole blood as a control material. It was found that fresh blood collected in disodium ethylenediaminetetraacetate alters hemorrhage in patients with acute leukemia more frequently than bank blood collected in acid citrate dextrose and stored at 5 C for 2 to 9 days. Favorable responses to fresh blood were observed in 10 of 14 bleeding episodes. Platelet levels after fresh-blood transfusion were significantly higher than those after bank-blood transfusion. However, all levels were well below the platelet level ordinarily associated with absence of hemorrhage (50,000 per cubic millimeter). The platelet levels after fresh-blood transfusion were not significantly different for those showing a clinical effect and those showing none.

SURGERY

An Analysis of the Pathologic Anatomy of Pulmonary Arteriovenous Aneurysms with Particular Reference to the Applicability of Local Excision. L. H. Bosher, D. A. Blake and B. R. Byrd. Surgery **45**:91-104 (Jan.) 1959 [St. Louis].

The authors analyzed the gross pathological anatomy of pulmonary arteriovenous aneurysms in 252 patients whose cases were collected from the world literature and in 98 patients whose cases have not been previously reported. The anatomic distribution of pulmonary arteriovenous aneurysms in the 350 patients showed a wide variability, ranging from multiple, diffuse, pulmonary telangiectasia to a single large aneurysm. Twelve cases are recorded in which a systemic artery joined the aneurysm. About 64% of the patients had single lesions, and in 75% the disease was unilateral. Angiography should be performed preoperatively in all patients to detect fistulas which are not visualized on plain chest roentgenograms. Of the 350 patients, 239 were operated on, and on 19 of these, bilateral resections were performed. There were 13 operative deaths. Seventeen patients, less than 10 years old, were operated on, and all but one of these obtained good results.

A technique for performing local excision of arteriovenous aneurysms in a bloodless field is reemphasized, and it is estimated that this can be employed in at least 50% of all cases, in preference to segmental resection or lobectomy. To illustrate the applicability of this technique, the case of a

39-year-old man with a large subpleural aneurysmal sac on the underface of the anterior segment of the left upper lobe is reported. The technique was utilized as follows: After occlusion of the main pulmonary artery and superior pulmonary vein together with the main bronchus, the sac was entered and the vascular orifices were observed, two of arterial origin, 6 mm. in diameter each, and one of venous origin, 1 cm. in diameter. The two arteries were ligated individually close to the base of the sac, but the large vein was dissected some distance proximally where it joined a vein from the anterior segment. The postoperative course of this patient was uneventful. Reexamination one year later revealed that he had gained 20 lb. (9.1 kg.) and that the previously noticed shortness of breath on exertion was no longer present. It is urged that surgeons should report any cases of late recurrence which might elucidate further the problem of latent small pulmonary arteriovenous fistulas.

Clinicopathologic Observations on the Fate of Arterial Freeze-Dried Homografts. A. W. Humphries, W. A. Hawk, V. G. de Wolfe and F. A. Le Fevre. Surgery **45**:59-71 (Jan.) 1959 [St. Louis].

The authors report on 525 patients with occlusive and aneurysmal disease, who were operated on and in whom arterial freeze-dried homografts were placed in the abdomen and in the lower extremity. In 31 patients the grafts were initially unsuccessful because of inadequate runoff. There was a total of 56 deaths; 4 of these were caused by technical failure of an inadequate proximal anastomosis in patients with aneurysm; of 10 patients who died as a result of failure of the homograft itself, 6 had local infections with resultant rupture of the graft, 2 died of erosion of the homograft as it pulsated against the cut end of the patient's own calcified vessel, and 2 died of rupture of a saccular aneurysm. Causes associated with major surgery, but not specifically with a graft, were responsible for the other 42 deaths. These included deaths due to myocardial infarction, rhythmic changes in the heart, usually ventricular fibrillation, and cerebral anoxia. A total of 438 patients thus were available for follow-up studies. Of these, 70 have incurred some incident in their postoperative course that has resulted in the loss of distal pulses and a presumed failure of the graft. In 368 patients the grafts remained successful for periods ranging up to 4½ years.

Of the 70 patients in whom late graft shutdown has occurred, 15 had aortoiliac and 55 had femoropopliteal grafts. All these patients had occlusive disease. Five had grafts which were lost through primary wound infections in the leg. These, combined with the 6 deaths due to infection, make a total of 11 infections (or 2%). In the presence of infection with associated proteolytic digestion of the homograft, the only safe procedure is to remove the graft, tie off the patient's own vessels, and abandon the project. Thirty of the late graft shutdowns were regrafted. Two of them were initially unsuccessful, a second late shutdown occurred in 2, and the remaining 26 regrafts are still potent and functioning. Most of the late graft shutdowns occurred in the femoropopliteal area due to the smaller caliber of the vessel, and most of the shutdowns occurred within the first year. Pathological findings in 33 grafts, 30 of which were obtained from regrafting and 3 from patients whose deaths occurred late, were as follows. Arteriosclerosis occurred in 7 of the grafts removed; multiple aneurysmal dilatation occurred in 1 case; arteriosclerotic aneurysm occurred in 1 femoral graft; saccular aneurysm developed in 4 grafts; 1 dissection occurred within a graft; and there were 11 instances of rupture due to infection.

Long-standing good results may be expected in those patients with aneurysm who survive the surgical intervention. One may also expect a certain acceptable percentage of late shutdowns in patients with occlusive disease, not necessarily of clinical importance, more in femoropopliteal than in aortoiliac grafts, which is in direct proportion to the size of the vessel, to degree of "activity" of disease, and undoubtedly to other as yet unknown factors. However, the longer a graft remains functional, the better the chances are that it will continue to remain functional.

Congenital Pulmonary Arteriovenous Fistula: Report of a Case and Review of the Literature. A. G. Fletcher Jr., K. Banerjee, T. Takaro and W. M. Bond. Indian J. Surg. **20**:416-422 (Oct.) 1958 (In English) [Madras].

The authors report on a 28-year-old man with pulmonary arteriovenous fistula for which he was operated on at the Wanless Tuberculosis Sanatorium in Miraj, India. There was a history of repeated attacks of pain in the lower chest on the left, but there was no history of cough, expectoration, or fever. Chest roentgenograms revealed a homogeneous circumscribed area of increased density in the left lower lung field toward the periphery. On fluoroscopy the lesion was shown to be anterior in position, probably in the lingula of the upper lobe. It was considered to be a circumscribed caseonecrotic focus or tuberculoma. The patient was given antimicrobial therapy for 6 months, on which he gained 17 lb. (7.7 kg.) in weight, but the lesion did not respond to therapy. A left-sided thoracotomy was performed, and on exposing the lung a soft, rounded, pulsating mass located just beneath the visceral pleura was found in the superior portion of the lingular segment. A strong thrill was palpable on slight compression of the lesion, which appeared to be a pulmonary arteriovenous fistula. Lingulectomy was performed to re-

move the lesion. The patient made an uneventful recovery and was free of symptoms when last seen one year after the operation. He apparently was the first patient operated on for pulmonary arteriovenous fistula and reported on in India. The cases of 40 patients with pulmonary arteriovenous fistula, who were operated on, were collected from the literature. There was only one postoperative death.

Pulmonary arteriovenous fistula is a relatively uncommon congenital defect with a hereditary tendency. The typical clinical picture is that of cyanosis and clubbing in a patient with a normal heart and a lung lesion revealed by chest roentgenogram. Polycythemia may be severe, but in some patients it may be absent or minimal. The diagnosis may be confirmed by laminography or angiocardiography. Dangerous complications reported by other workers were hemoptysis, hemothorax, brain abscess, bacterial endarteritis, and cerebral thrombosis. The treatment of choice is surgical resection of the involved portion of the lung after carefully checking for multiple lesions.

Intra-Aortic Blood Transfusion. V. S. Ermakov. Khirurgiya **34**:23-27 (no. 11) 1958 (In Russian) [Moscow].

The author reports on 10 cases in which transfusion of blood into the abdominal aorta was employed in grave surgical shock and in blood loss. A good and stable effect was seen in 7 patients who recovered; an effect of short duration was obtained in 2 patients. The author's observations show that the intra-aortic transfusion of blood is a powerful therapeutic measure which may be employed in prophylaxis and in combating severe shock. The rise in arterial blood pressure and an improvement in the cardiac activity and respiration appeared directly after the injection of the first portions of blood. The total amount of blood injected in shock was 70 to 140 ml., while in shock combined with blood loss it was 250 to 300 ml. The author suggests a special method for intra-aortic blood transfusion, which enables one to control the aortic blood pressure and, consequently, to determine the required amount of blood for the achievement of the effect.

Spasm: A Preliminary Clinical Report on a Non-destructive Method for the Relief of So-Called "Mass-Reflex" Spasm. D. Munro and E. L. Spatz. New England J. Med. **260**:1-6 (Jan. 1) 1959 [Boston].

This paper deals only with the so-called mass-reflex spasm. This occurs solely in connection with injuries of the spinal cord between the 3rd cervical and 1st sacral segments. Of the 3 characteristics of the mass-reflex spasm, the first is an excessive, self-propagating, maximal motor response to a minimal sensory stimulus. Muscular overresponse takes the form of a strong, spastic, slowly released movement of the various parts of the limb at the individual joints. The motion may be either pure flexor, pure extensor, alternate, or mixed. If the spasm causes pure flexion, the great toe is first dorsiflexed, followed by fanning of the other toes and dorsiflexion of the ankle. This activity is rapidly propagated without further external stimulus to the flexors of the knee, then to the adductors of the thigh, the flexors of the thigh, and the paraspinal and psoas muscular groups with flexion at the waist; if the cord injury is high enough, there is a spread to the abdominal muscles, as well as the adductors and flexors of the arm, forearm, and hand.

If not corrected, and as the various muscle groups are involved one by one, the position of the legs and body becomes firmly fixed in either flexion, if the spasm started as pure flexor spasm, or extension, if it started as pure extensor spasm. Mixed flexor-extensor spasm will present a confusing picture of limb fixation, but the basic self-provocative nature, progression, and distribution will be present in any case. The second characteristic of the mass-reflex spasm is its tendency to form a vicious circle as the result of repeated sensory stimuli, which originate in the area of muscle and tendon contractions and which, in turn, produce more muscle responses out of which arise, in their turn, more motor-producing sensory stimuli. The third characteristic is the semi-isolated reaction, which involves in its own vicious circle the bladder, the external urethral sphincter, the rectum, and the anal canal.

A previously unreported method designed to eliminate the mass-reflex spasm in patients with spinal-cord injuries is reported. This method has been based upon the hypothesis that such spasm differs from other spasms in that, in its pure form, it is self-propagating from the periphery, progresses centrally, and has circular form. The urinary bladder, the external urethral sphincter, and the intestine-emptying mechanism are all adversely affected by the mass-reflex spasm and may remain so after the skeletal-muscle spasm is abolished. This visceral spasm is also self-propagating and circular in form. Permanent abolition of spasm of the detrusor and external urethral sphincter can be brought about by properly placed procaine and, rarely, by alcohol injections of the sciatic roots through the sacral foramens in the former condition and by injection of procaine into the internal pudic nerves in the latter condition. Destructive permanent denervations, whether surgical or chemical, of the parasympathetic and somatic nerve supply to the bladder and the external urethral sphincter, as well as destruction of the urethra by punch operation, are not necessary and are practically always contraindicated. Previous abolition of skeletal mass-reflex spasm is an essential prerequisite if this therapy is to succeed. Selective

anterior-rootlet rhizotomy may be indicated in certain especially selected cases as a method for reducing the mass-reflex spasm.

Injection with procaine, or its derivatives, of the sciatic nerve in the thigh and of the ulnar, median, and radial nerves in the arms shows promise of further success in the control of spasm associated with partially injured spinal cords even in quadriplegic patients. The sciatic nerves should be exposed for injection through a posterior upper-thigh approach at the first injection. The procaine solution should be injected under direct vision into the nerve trunk. The epineural sheath must not be incised. Silver clips should be so placed as to indicate the place and plane of future injections, which should then be done with fluoroscopic guidance of the injecting needle. The ulnar, median, and radial nerves should all be exposed for injection under direct vision at the level in the arm where they surround the brachial artery. The physiological implications of the control of abnormal postural reflex activity, as demonstrated in the cases reported, warrant further investigation.

Symptomatic Myelolipoma of the Adrenal Gland: Report of a Case and Review of the Literature. L. Parsons Jr. and J. E. Thompson. New England J. Med. **260**:12-15 (Jan. 1) 1959 [Boston].

Myelolipoma of the adrenal is rare, and so far has been described only as an incidental finding at autopsy. The case reported here is of interest, because the authors believe it to be the first recorded case in which a myelolipoma reached a large enough size to produce symptoms necessitating operative removal. The patient was a 51-year-old woman, hospitalized in October, 1956, with a 2-month history of malaise, anorexia, and poorly localized discomfort in the upper abdomen. These symptoms were increasing. In the month before admission there had been occasional nausea and vomiting, as well as a 5.4-kg. (12-lb.) weight loss. The discomfort was unrelated to foods. Intermittent headaches were a complaint of long standing. In the right upper quadrant of the abdomen there was a large, rounded mass extending 5 finger-breadths below the costal margin in the midclavicular line. The mass was slightly tender; it moved with respiration and with manipulation.

At exploratory operation, the colon was seen to overlie a large retroperitoneal mass. The retroperitoneal space was entered, and an ovoid tumor was seen lying on the vena cava just above the right kidney. Mobilization of the tumor was readily performed, except at its upper pole where it was contiguous with a thinned-out rim of adrenal tissue. The patient made an uneventful recovery, with relief of the symptoms. There has been no evidence of recurrence. The specimen was a large, oval mass, 25 cm. long, 13 cm. wide, and 12 cm. thick. It weighed 1,250 Gm. Sectioning of the growth revealed adipose tissue, the structure and organization of which were similar to those seen in lipomas in general. The adipose tissue was traversed by bundles of fibrous tissue. The purplish areas observed on gross examination represented, variously, adipose tissue, markedly congested sinusoids, fresh and old hemorrhages, and occasional clusters of lymphocytes, as well as bone-marrow tissue with hematopoietic elements. The peripheral orange-yellow tissue described on gross examination was adrenocortical tissue beneath a fibrous capsule. No adrenal medulla was seen in the many sections examined.

The Use of Intravenous Pituitrin in Treatment of Bleeding Esophageal Varices. S. I. Schwartz, H. W. Bales, G. L. Emerson and E. B. Mahoney. Surgery **45**:72-80 (Jan.) 1959 [St. Louis].

The authors treated 11 patients with acutely bleeding esophageal varices by intravenous administration of a commercial posterior pituitary preparation (Surgical Pituitrin) or a commercial preparation of vasopressin injection (Pitressin). The estimated blood loss before the institution of therapy varied between 250 and 1,000 cc. Ten of the 11 patients had alcoholic cirrhosis. A Levin nasogastric tube or an uninflated Sengstaken-Blakemore tube was inserted in 9 of the patients in order to maintain a constant gastric suction and thus decrease regurgitation into the esophagus of gastric fluid. Twenty clinical units of Surgical Pituitrin or Pitressin, usually diluted with 200 cc. of 5% dextrose in distilled water, were administered over a half-hour period, and the nasogastric tube irrigated at half-hour intervals. Rapid infusion is necessitated by the tachyphylactic property of the drugs. Therapy can be repeated at 4-hour intervals if there is evidence of continued or recurrent bleeding. In the group of 9 patients, 25 distinct episodes of acute bleeding were so treated, with prompt control 22 times. The gastric aspirate cleared 5 to 20 minutes after the completion of the intravenous administration of Surgical Pituitrin or Pitressin. In 2 patients in whom transthoracic esophagotomy resulted in brisk "arterial"-type bleeding, which obscured the surgical field and made identification of the individual varices extremely difficult, 20 units of Surgical Pituitrin were administered over a period of 3 minutes, with a dramatic reduction in the intensity of the bleeding, thus making the individual varices more apparent for suture.

Surgical Pituitrin and Pitressin are worthwhile additions to the therapy of bleeding varices. Direct portal venous pressure measurements in patients with esophageal varices have shown that intravenously administered Surgical Pituitrin results in a rapid and marked lowering of portal pressure, equivalent to the level achieved by portacaval

shunt. The drugs have proved effective in the control of acutely bleeding esophageal varices and have been helpful in facilitating transesophageal ligation of bleeding varices. It is recommended that an intravenous regimen with Surgical Pituitrin or Pitressin be given an initial trial in the control of bleeding in view of the distinct advantages over balloon tamponade.

Anastomosis Between the Subclavian Artery and the Aorta in Surgical Treatment for Coarctation of the Aorta. T. De Nunno and R. Gentilli. Minerva cardioangiol. **6**:513-518 (Oct.) 1958 (In Italian) [Turin, Italy].

A successful anastomosis between the subclavian artery and the aorta, according to the technique of Blalock, was performed on 4 patients with coarctation of the aorta, aged between 16 and 30 years. The considerable length of the constricted segment of the aorta in 3 patients and a laceration of the upper segment of the aorta which occurred during operation made unfeasible an end-to-end anastomosis between the 2 segments of the aorta. Interruption of the subclavian artery did not cause trophic disturbances in the contiguous upper extremity because of an abundant collateral blood supply. The blood supply of the lower extremities was also adequate, being confirmed by preoperative and postoperative blood pressure recordings. The arterial blood pressure was about 210/90 mm. Hg in the upper left extremity and about 100/90 mm. Hg in the lower extremity before the operation. These values approached each other closer in these patients after the operation, being approximately 140/80 mm. Hg in the upper extremities and the same or slightly lower in the lower extremities 10 days after the operation. The patients were well 2 months after the operation. Vertigo, headache, and head pulsation disappeared in those instances in which they were present before the operation, and blood pressure in the lower and upper extremities showed insignificant changes from previous recordings. Anastomosis between the subclavian artery and the aorta thus permitted the reestablishment in this series of patients of a circulatory condition close to the normal pattern.

Development of Primary Pyloric Hypertrophy in Adults in Relation to the Structure and Function of the Pyloric Canal. S. C. Skoryna, H. S. Dolan and A. Gley. Surg. Gynec. & Obst. **108**:83-92 (Jan.) 1959 [Chicago].

Adults with pyloric hypertrophy exhibit ill-defined but somewhat ulcer-like symptoms. The variable symptomatology and difficulty in distinguishing with absolute certainty between benign pyloric stenosis and malignant tumors of this region account for the fact that a proportion of these cases will continue to be undiagnosed before surgical exploration. The authors call particular attention to the relationship of the development of primary pyloric hypertrophy in adults to the structure and function of the pyloric canal. The histories of 6 adults with pyloric hypertrophy, who were studied in the department of surgery of St. Mary's Hospital and of the Royal Victoria Hospital, Montreal, are presented. Their ages ranged from 31 to 61 years. All were operated on, and the diagnosis of pyloric hypertrophy was confirmed by histopathological studies. The structure of the pyloric canal is described on the basis of anatomic findings. The structure of the circular musculature of the pyloric canal appears to be of primary significance in this region. It consists of circular muscle fibers forming a distal (pyloric) loop and a proximal (intermediate) loop enclosing an area of circular fibers which are parallel on the greater gastric curvature side and by convergence form a muscle torus on the lesser curvature. It is concluded that the development of the primary pyloric hypertrophy in adults is related to this structure of the circular muscle layer of the pyloric canal. The physiological evidence for the existence of a pyloric canal mechanism rather than of a pyloric sphincter is discussed.

Primary pyloric hypertrophy in adults is divided into (1) a focal form (torus hypertrophy), (2) a diffuse form associated with proximal lesions, and (3) a diffuse form without other lesions. It is suggested that a congenital neuromuscular dysfunction of the pyloric canal mechanism forms a common basis for both the infantile and the adult pyloric hypertrophy. The relative incidence of each form appears to be determined by the extent of the normal regression in the circular musculature of the pyloric canal during early infancy and by the action of secondary factors during adult life.

Perforated Gastric-Duodenal Ulcers and Their Treatment. M. Pastori. Minerva chir. **13**:1263-1267 (Nov. 15) 1958 (In Italian) [Turin, Italy].

The author reports on 119 patients with peptic ulcer who had received surgical treatment since 1937. Duodenal ulcer was present in two-thirds of the patients. The average age of the patients was 35 years. The series included only 4 female patients. The greatest incidence of the disease was observed in spring and in autumn. Perforation was treated by gastroenterostomy in 32 patients (mortality rate, 25%), by resection in 7 (mortality rate, 28%), and by simple suture in 80 (mortality rate, 12.5%). Gastroenterostomy had been used earlier but recently gave way to other surgical methods. There were no deaths among 32 patients treated recently by a simple suture. For this reason the author has selected simple suture, complemented by continual aspiration before and after the operation, as the procedure of choice in the treatment of perforated ulcer. Gastric resection, though, remains

the most efficacious surgical procedure for treatment of ulcerous disease in the course of its normal development.

The Management of Massive Hemorrhage from Diverticular Disease of the Colon. C. M. Earley Jr. Surg. Gynec. & Obst. **108**:49-60 (Jan.) 1959 [Chicago].

This report reviews observations on 23 patients with massive bleeding associated with diverticular disease of the colon, who were treated at the Medical College of Virginia Hospitals, Richmond, from January, 1952, to August, 1957. They represented 4.5% of the 486 patients diagnosed during this time as having diverticulosis. No attempt was made to study patients with occult or minimal bleeding. Rather, this article is concerned with bleeding sufficiently massive to be noticed by the patient and to cause him to seek medical attention. Other possible causes for the bleeding must be ruled out. The ages of the 23 patients ranged from 44 to 81 years, the average age being 65 years. There were 14 women and 9 men. Hypertensive cardiovascular disease was present in 13. One patient had 4 hospital admissions with massive bleeding; 5 others had 2 admissions each. Data on all 23 patients are tabulated, and 8 especially interesting case histories are described in detail.

The initial care is conservative, with supportive therapy including adequate blood replacement. Most patients will respond to it and cease to bleed quite as suddenly as they began. The average volume of blood administered to the 16 patients managed conservatively was 1,000 cc. per hospital admission. The 7 patients requiring surgical treatment for control of hemorrhage received an average of 6,000 cc. of blood each. A review of the literature revealed a total of 23 patients who were treated surgically in order to control hemorrhage from colonic diverticular disease. Most of these procedures were performed as emergencies, and most of the patients were over 60 years old. At operation, all of the colon containing diverticula should be resected, unless the actual bleeding point can be identified. In a bleeding patient too critically ill to tolerate resection or colectomy, proximal ileostomy or colostomy may be helpful, although there is no certainty that the bleeding will stop after this procedure.

Fibrinolysis and Hypofibrinogenemia: Three Cases. P. H. Sørensen. Ugesk. laeger **120**:1669-1674 (Dec. 11) 1958 (In Danish) [Copenhagen].

Fibrinolysis is thought to originate by the introduction of lysokinase into the blood stream, by the release of tissue activators, or by inactivation of inhibitors. Hypofibrinogenemia may be a result of the fibrinolysis, which can cause a fibrinogen consumption increased beyond the production ability of the liver. In the same way a powerful stimulation of the coagulation process on release of tissue thromboplastin can cause hypofibrinogenemia. Finally, there may be so strong an effect on the liver that reduced liver function and hypofibrinogenemia result. The first of the cases reported was that of a woman, aged 60 years, with cancer of the stomach and extensive metastases. Profuse bleeding from the urinary tract developed. Hypofibrinogenemia and fibrinolysis were established. In spite of blood transfusion and administration of plasma and fibrinogen, the patient died 5 days after the beginning of the bleeding. In a multipara, aged 33 years, admitted because of premature separation of the placenta, there were shock, fibrinolysis, and slight hypofibrinogenemia. Treatment with dextran, blood, fibrinogen, and pitupartin was applied; the patient recovered. In the third instance, in a man, aged 60 years, with metastasizing cancer of the prostate, afibrinogenemia and fibrinolysis leading to cutaneous and cerebral hemorrhage developed shortly before death.

Debricin—Clinical Experiences with a New Proteolytic Enzyme in Surgical Wounds. J. F. Connell Jr., L. R. M. Del Guercio and L. M. Rousselot. Surg. Gynec. & Obst. **108**:93-99 (Jan.) 1959 [Chicago].

During the past 7 years the burn research group at St. Vincent's Hospital, New York, has been evaluating many enzymatic materials for wound débridement. Debricin proved to be the material that best fulfilled the requirements of an ideal wound débridement agent. This enzymatic agent was developed from ficin in the sap of the fig tree. While highly active against fully denatured protein, the material is only partially active on marginal necrotic tissues. There has been no evidence of systemic toxicity and very little evidence of wound maceration. The powdered material comes mixed with a buffer, and it is activated by mixing the enzyme into a special jelly base. The dry material is stable indefinitely, and, after mixing, the refrigerated material is stable for at least 7 days. The buffered enzyme is most active at pH 5.4. Dilution by strong acid or base producing organisms or antibiotics will tend to be inhibitory.

The material must be applied so that the enzyme-substrate contact is kept at a maximum, and reapplied at 12-to-24-hour intervals to remove inhibitory by-products. There is little difficulty in applying the enzyme to postoperative wounds, deep ulcers, fistulas, sinus tracts, or chest cavities, but flat surface areas, such as shallow ulcers or burns, will tax the surgeon's ingenuity. The best method for the flat surface lesions is to spread the enzyme in a jelly base thickly over the area, cover this with a petrolatum gauze or polyvinyl sheet, and overlay the whole with a thick, absorbent pad. A second

method of treating the flat surface eschar is to apply the enzyme as a wet dressing, suspending the buffered material in 100 cc. of isotonic sodium chloride solution and instilling it every 3 to 5 hours through rubber catheters tunneled in an absorbent pad overlying the eschar. The outer surface of this pad should be covered by a polyvinyl sheet to limit evaporation.

The main purpose of using the enzyme is to clean a wound of necrotic tissue elements and to thin out thick exudative collections. The authors used Debricin in 139 patients with a variety of surgical lesions. They found that there is rapid, complete débridement when the enzyme is properly used on various types of ulcerations, deep burns, sinus tracts, and wound infections. Debricin used topically is nontoxic. Antibiotics should be utilized during the course of therapy. The enzyme improves the conditions for healing by its cleansing activity. Its use should be followed by the appropriate surgical procedure to obtain wound closure when indicated. Further studies on local enzyme-antibiotic combinations are in progress.

PEDIATRICS

Esophageal Stricture from Accidental Ingestion of Clinitest Tablets. C. Zimmerman. A. M. A. J. Dis. Child. **97**:101-103 (Jan.) 1959 [Chicago].

The author presents the history of a 3½-year-old girl, who was admitted to the Bronx Municipal Hospital Center, New York, on Aug. 6, 1957. The patient began vomiting intermittently 3 weeks prior to admission, about 1 week after a visit to her maternal grandmother, a diabetic. This vomiting progressed, as did anorexia and weight loss, until admission. The vomitus consisted of partially digested food. Physical examination was negative. On the third hospital day the grandmother volunteered the information that the patient had swallowed a Clinitest tablet which was used in urine testing. On the fourth hospital day an esophagogram revealed a stricture of the esophagus just above the level of the carina. Esophagoscopy showed the stricture, and a tube gastrostomy was done. When esophagography was repeated later, it showed complete obstruction at the stricture site. After unsuccessful attempts at dilatation, the stenotic segment was resected, and an end-to-end anastomosis was performed. Four weeks after surgery the patient was eating strained bulky foods.

Four other cases of esophageal stricture caused by Clinitest tablets were found in the literature. Three of these involved children; one also had a complete stricture. An esophagogram will confirm the clinical impression of esophageal stenosis or stricture. If the patient has contact with a diabetic and no etiology is apparent, ingestion of Clinitest should be considered. This tablet can cause a partial or complete stricture of the upper esophagus because of the action of the lye constituent. The copper sulfate content may play a secondary role.

The Infant of the Diabetic Mother. S. S. Gellis and D. Y-Yung Hsia. A. M. A. J. Dis. Child. **97**:1-41 (Jan.) 1959 [Chicago].

Despite its large size and apparent maturity the infant of the diabetic mother behaves much like a premature infant and is very frail. About a third of such infants die either in utero or in association with respiratory distress during the early neonatal period. In the 3 decades since the discovery of insulin the problems of the diabetic mother and her infant have received much attention. The authors evaluate the work previously done in this field, and they add observations made on 934 pregnancies of diabetic women in the Joslin Clinic, Boston, between 1940 and 1956. The women were seen in the clinic during pregnancy and were subsequently delivered at the Faulkner Hospital (1940-1950) and the Boston Lying-in Hospital (1950-1956). All the patients were under the care of a team consisting of an internist, 2 obstetricians, an anesthetist, and a pediatrician.

Pregnancy failures were several times commoner in women with diabetes mellitus than in healthy women. This excessive loss was limited mostly to the period after the 28th week of gestation. Comparison of mortality figures showed no significant decrease in the fetal mortality in recent years. Experience and teamwork in therapy seemed to influence the ultimate outcome of such pregnancies. Two maternal factors appeared to influence the fetal mortality: (1) severity of maternal disease and (2) good diabetic control. While there is evidence that diabetic women have a hormonal imbalance during pregnancy and that this is frequently associated with the death of the fetus, there is no proof that female sex hormones either correct this defect or significantly reduce the fetal mortality rate.

Infants of diabetic mothers should be delivered between the 35th and the 36th week of gestation. This prevents the high mortality rate associated with prematurity if delivery takes place too early and the marked increase of stillbirth if delivery takes place closer to term. There is no evidence that the mode of delivery or the type of anesthesia used significantly affects the outcome. Respiratory distress is the principal complication. At postmortem examination, pulmonary hyaline membranes and atelectasis have been the only findings in two-thirds of the infants who die. Hypoglycemia, infections, and congenital anomalies play a minor role in the high neonatal mortality rate. The use of antibiotics, oxygen, mist, or cortisone is not helpful in either the prevention or the treatment of hyaline-membrane disease in these infants. Instead, one has to rely on good pediatric care and

general supportive measures. No rational mode of treatment for the infant of the diabetic mother is likely to emerge until the maternal and fetal factors which are responsible for the pathogenesis of pulmonary hyaline membranes are better understood.

Acute Ataxia of Childhood: A Summary of 15 Cases. G. M. Lasater and J. T. Jabbour. A. M. A. J. Dis. Child. **97**:61-65 (Jan.) 1959 [Chicago].

Acute cerebellar ataxia is usually a benign disorder subsiding in a few days or weeks. It rarely occurs in adults. The etiology is often undetermined, but in most cases it is thought to be a cerebellar encephalitis of infectious or toxic origin. The authors present a summary of the clinical picture and a discussion of possible etiologies based on reports in the literature and their own observations of 15 cases. The ages of the 15 children ranged from 2 to 12 years, all but 2 being less than 8 years old. The most characteristic clinical feature is the abrupt onset of a grossly ataxic gait. This often occurs in a previously well child and sometimes during the convalescent phase of one of the childhood viral infections. The usual story is that the child awoke in the morning or from his afternoon nap and fell upon attempting to walk. It is then discovered that he walks with a staggering gait, falling frequently. Some patients have intention tremors of the upper extremities. Occasionally nystagmus, dysarthria, hypotonia, and dysmetria are also demonstrated. At times there are signs of dysfunction in other parts of the nervous system, such as lethargy, cloudy sensorium, myoclonic movements, and cranial nerve palsies. There is usually no nuchal rigidity. Fever, nausea, and vomiting may be present. The spinal fluid is often normal but may contain a moderate excess of mononuclear cells and protein. Recovery occurs within 1 week to 8 months, usually in 1 to 3 weeks.

Observations on the 15 children suggested mumps, poliomyelitis, influenza, varicella, and intoxication from insecticides as possible etiological agents. Acute ataxia has also been reported in association with rubeola, rubella, smallpox, scarlet fever, typhoid, infectious mononcleosis, diphtheria, and drug intoxication. The prognosis for complete recovery is good.

Occasionally, symptoms caused by a cerebellar tumor may develop acutely, and this lesion must always be considered in children with acute ataxia. Headache and vomiting are more common with cerebellar tumors, but signs that should especially alert the clinician to the probability of this diagnosis are papilledema, tilting of the head, unilateral dysmetria, nystagmus which is more marked in one direction, 6th nerve palsy, high spinal fluid pressure, and x-ray findings of separation of the sutures, erosion of the clinoid processes, and increased convolutional markings.

The Antibiotic Prophylaxis of Bacterial Complications of Measles. S. Karelitz and H. D. Isenberg. J. Pediat. **54**:1-10 (Jan.) 1959 [St. Louis].

A total of 251 children with measles were observed, 173 of them at home and 78 at the Queens General Hospital in Jamaica, N. Y. The ages of these children ranged from 1 to 14 years. Of the 78 hospitalized children, 31 had complications, such at tracheobronchitis, pneumonia, and nonbacterial encephalitis. Antibiotic prophylaxis was given to only 2 children before hospitalization; the remaining 76 children had no antibiotic prophylaxis before their admission to the hospital. While at the hospital the antibiotic therapy, consisting of penicillin or erythromycin, was given to a total of 51 patients, 25 of whom had complications and 26 had none. All the hospitalized patients recovered, whether they were subjected to antibiotic therapy or not. Of the 26 patients who were hospitalized without complications and who were subjected to antibiotic treatment, only one developed a secondary infection; this one child who had been given a diagnosis of measles was found to have influenzal meningitis on the 5th hospital day.

Of the 173 children with measles observed at home, the antibiotic therapy was administered to 88, and the antibiotic prophylaxis to 18. Complications occurred 1 to 11 days after the antibiotic treatment had been discontinued in 14 of the 88 patients. These complications included pneumonia in 1 patient, bronchitis in 1, and otitis media in 12. No complication was manifested during the prophylactic treatment. Complications, such as otitis media and pneumonia, occurred in 18 patients who were not subjected to prophylactic treatment.

The higher complication rate observed in the hospitalized children may be attributed to (1) the difference in the social environment of the 2 groups, (2) the younger age of the children, and (3) the complications already manifested by the children at the time of their hospitalization. The authors emphasize the importance of the prophylactic use of antibiotics in very young and weak children with measles in whom the occurrence of complications could be a threat.

Intravascular Red Cell Aggregation in Children with Heart Disease. F. Arajärvi. Ann. paediat. Fenniae. **4**:249-255 (no. 4) 1958 (In English) [Helsinki].

A method is available which makes it possible to observe conjunctival blood vessels and the blood cells circulating in them with the aid of a capillary microscope. In healthy adults and children the red blood cells flow along in the smaller vessels in single or double files; in the larger vessels they flow in a homogeneous mass. In many abnormal conditions, though, the red blood cells adhere in

clumps; this adherence is visible in the conjunctival blood vessels as a break-up of the files in the smaller vessels and as definite clumps in the larger ones. The author tried to find answers to the following questions: 1. Do vascular disturbances due to congenital heart disease cause aggregation of the red blood cells? 2. Is there any noticeable difference in the appearance of the intravascular aggregation of the red blood cells if the child has a congenital heart disease or rheumatic fever? 3. Is this method of investigation helpful in the cyanotic newborn infant, particularly in the detection of congenital heart disease?

With the aid of a stereomicroscope, conjunctival blood vessels and the blood cells circulating in them were examined in 96 children. In 48 children with congenital heart disease, no red blood cell aggregation was present unless the child had also an infection, but in 23 children with active carditis, red blood cell aggregations could be found. When the conjunctival blood vessels of 20 newborn infants who were cyanotic were examined with the stereomicroscope, red blood cell aggregations could be found in those who had infections (pneumonia, encephalitis) or brain hemorrhage, but no red blood cell aggregations were found in those with congenital heart disease. This proves that this examination is of value in the differential diagnosis of cyanosis in newborn infants.

Intravascular Red Cell Aggregation in Children with Benign and Malignant Tumors. T. Arajärvi and G. R. Wallgren. Ann. paediat. Fenniae. **4**:256-263 (no. 4) 1958 (In English) [Helsinki].

The studies described in this paper were carried out to ascertain: (1) whether a tumor can cause red blood cell aggregation; (2) whether there is any difference in this respect between a benign or a malignant tumor; and (3) whether the aggregation test might be an aid in the early diagnosis of cancer. The stereomicroscope was used in the study of the red blood cells circulating in the conjunctival blood vessels of 100 children who had been hospitalized because of a proved or suspected tumor. The diagnosis was confirmed in all the children by histopathological examination. Red blood cell aggregation was very mild or completely absent in the children with benign tumors or with congenital anomalies. In the children with malignant tumors the red blood cell aggregation was definite. However, aggregation of red blood cells was present also in children who had an infection in addition to a benign tumor or who had only an infectious disease instead of the suspected tumor. The degree of the red blood cell aggregation was proportional to the increase in the sedimentation rate and to the decrease in the hemoglobin value in the children with malignant tumors.

DERMATOLOGY

Chronic Penicillin Urticaria from Dairy Products, Proved by Penicillinase Cures. M. C. Zimmerman. A. M. A. Arch. Dermat. **79**:1-6 (Jan.) 1959 [Chicago].

Penicillin is widely used to treat mastitis in cattle. From this use it contaminates, according to an estimate made in 1957, 11% of American milk samples. The contamination of dairy products by traces of penicillin has previously been suspected but never proved as a cause of allergic reactions. The author reports on 3 men and 1 woman in whom proof of the allergenicity of penicillin in dairy products has been based on the following evidence: 1. All the patients had previous allergic reactions (urticaria) to penicillin. 2. The previously known allergic reaction to penicillin was duplicated repeatedly after ingestion of dairy products. 3. The reaction cleared rapidly after injection of 800,000 units of penicillinase (Neutrapen), a penicillin-destroying enzyme with no effect on anything but penicillin. 4. The patients were able to eat dairy products without subsequent allergic reaction if given a prophylactic injection of penicillinase first.

Patients with chronic urticaria in whom penicillin sensitivity is suspected should be given a test injection of penicillinase. If urticaria clears for 4 to 7 days, penicillin sensitivity has probably been the cause. Patients with chronic urticaria, in whom penicillin sensitivity is proved or suspected, should have such dairy products as milk, ice cream, and Roquefort or bleu cheeses containing Penicillium species molds eliminated from their diets. If patients have a flare-up 4 to 7 days after a penicillinase injection, there is residual penicillin in the system which has not been destroyed. Penicillinase injections should be repeated at 4-to-7-day intervals, as necessary, to stop symptoms. If more than 8 days pass before a new outbreak of allergic symptoms after an injection of penicillinase, then the penicillinase has destroyed all the penicillin in the system at that time. A new outbreak suggests either that the patient has had a new exposure to penicillin or that his new reaction is due to some other allergen.

Smooth-Muscle Tumors of the Skin. H. Montgomery and R. K. Winkelmann. A. M. A. Arch. Dermat. **79**:32-41 (Jan.) 1959 [Chicago].

The authors report on 33 patients with smooth-muscle tumors of the skin on whom biopsies were performed at the Mayo Clinic. Of the 33 patients, 23 had leiomyoma cutis, 8 had angiomyoma, 1 had nodular or so-called dartoic myoma, and 1 had leiomyosarcoma. The ages of the 8 male and 15 female patients with leiomyomas ranged from 10 to 20 years at the time of onset of the clinical signs. The lesions were located on the face, trunk, or extremities; they progressed slowly and became pain-

ful when they were large enough to invade and extend around the bundles or trunks of cutaneous nerves in the deeper part of the cutis and the subcutaneous tissue. Special stains did not reveal any increase in nerve fibrils or nerve trunks. Special histochemical stains proved to be of little value in identifying myomatous tissue. All the angiomyomas occurred as solitary lesions, and all the 8 patients were women. The age of onset was much later in this group than in that with leiomyomas, which sometimes began at birth or shortly thereafter. Dartoic myoma, which occurred in the scrotum of a 54-year-old man, is an uncommon lesion seen primarily by the surgeon because it begins in the subcutaneous tissue and calls for surgical removal. A painful leiomyosarcoma of one year's duration was removed surgically from the right thigh of a 32-year-old woman; the patient apparently had no recurrent tumors 21 years after the surgical excision. Smooth-muscle tumors may be allowed to remain in situ as long as they are asymptomatic. When treatment is desirable, surgical excision is the method of choice. Radiotherapy apparently has no effect on the lesions or the sensations that they produce.

Granuloma Faciale. W. C. Johnson, R. S. Higdon and E. B. Helwig. A. M. A. Arch. Dermat. **79**:42-52 (Jan.) 1959 [Chicago].

The authors report on 14 men and 1 woman with granuloma faciale, a dermatosis characterized clinically by elevated, usually asymptomatic, reddish-brown plaques on the face. Tissue sections from the lesions of these patients were examined at the Armed Forces Institute of Pathology for the purpose of determining the natural history of granuloma faciale and its relation to eosinophilic granuloma and of exploring its histogenesis. In 12 of the 15 patients the clinical aspect of the disease was that of a plaque or nodule, and in the remaining 3 it was that of a macula. The lesions were soft, usually brown, red, or purple, and varied from a few millimeters to 8 cm. in diameter. New lesions developed over a period of several months in some of the patients. Five patients were asymptomatic, but 10 noticed varying degrees of itching, burning, stinging, or tenderness. Response to therapy other than wide excision was poor. The lesion in most patients tended to persist indefinitely but varied in color and substance from time to time. The general health of the patients remained good.

No evidence was found of any relationship between granuloma faciale and eosinophilic granuloma of bone or the heterogeneous conditions once called eosinophilic granuloma. The authors' observations suggest that the pathogenesis of granuloma faciale is basically an antigen-antibody or hypersensitivity reaction, the small blood vessels and perivascular tissues in the upper corium of the face being the "shock" tissues. The exciting factors remain unknown, but foci of infection, photosensitivity, trauma, and drugs must be considered.

Genetic Studies on Acanthosis Nigricans. H. O. Curth and B. M. Aschner. A. M. A. Arch. Dermat. **79**:55-66 (Jan.) 1959 [Chicago].

The authors carried out genetic studies on patients with acanthosis nigricans at the department of dermatology of the College of Physicians and Surgeons of Columbia University in New York. Three types of this dermatosis have been recognized, namely, benign acanthosis nigricans, malignant acanthosis nigricans, and pseudoacanthosis nigricans. Family studies of 13 patients with the benign type of the disease revealed 9 families in which more than one member was affected. Altogether, there were 27 instances of benign acanthosis nigricans in these 9 families, 14 of the patients being males and 13 females. These figures suggest a genetic background for the benign type of acanthosis nigricans, which shows either regular or irregular dominance. Pseudoacanthosis nigricans, secondary to excessive obesity, may be considered a phenocopy of benign acanthosis nigricans. Pseudoacanthosis nigricans was not included in the authors' genetic studies because environmental factors, such as food intake and personal hygiene, seem to have played a significant role in the pathogenesis of the disorder.

No familial case of malignant acanthosis nigricans has been found. Family studies of 26 patients with the malignant type of the disorder revealed one consanguineous marriage among the parents of the 26 patients. The series of families studied is too small to permit this incidence to be considered as an indication of recessive inheritance of malignant acanthosis nigricans. Family members of patients with malignant acanthosis nigricans were examined also for cancer without acanthosis nigricans. No specific trend with regard to frequency and location of tumors in the relatives of the 26 probands was seen, and cancer did not occur in the relatives of 14 (54%) of these probands. In 24 of the 26 probands with malignant acanthosis nigricans, the two parents in each case had an identical ethnic background. The possibility of a genetic basis for the whole syndrome of malignant acanthosis nigricans, as for part of it, has been discussed. The tumors associated with maligant acanthosis nigricans, although originating in various organs, show similar clinical behavior and similar morphology in that they all are adenocarcinomas; the specificity of these tumors, however, has not as yet been established. The percentage of gastric cancers among the cancers associated with malignant acanthosis nigricans has been high. The fact that no instance of transition from the benign to the malignant form or of occurrence of both types in

one family has ever occurred confirms the assumption that benign and malignant acanthosis nigricans are separate diseases.

Fungistasis of Hydrocortisone and Certain of Its Analogues. R. L. Sauvan and R. L. Sutton Jr. A. M. A. Arch. Dermat. **79**:53-54 (Jan.) 1959 [Chicago].

The authors tested the fungistatic properties in vitro of hydrocortisone acetate and hydrocortisone alcohol in 0.1 and 0.9% concentrations and of prednisolone phosphate and prednisolone alcohol in 1.0% concentrations. The organisms selected for testing were common dermatophytes: Trichophyton rubrum, T. gypseum, Microsporum audouini, M. canis, and Candida albicans. Results of the tests showed that the hydrocortisones and the prednisolones in the concentrations used did not display fungistatic properties against the fungi tested. C. albicans grew well under conditions adverse to the growth of T. gypseum, M. audouini, T. rubrum, and M. canis.

OTOLARYNGOLOGY

The Auditory Manifestations of Leukemia. E. Shanbrom and S. C. Finch. Yale J. Biol. & Med. **31**:144-156 (Dec.) 1958 [New Haven, Conn.].

The records of the last 100 patients with leukemia admitted to the Yale-New Haven Medical Center were reviewed for evidence of acoustic difficulties. All patients with leukemia, irrespective of age, sex, and type of leukemia, were included. Thirty-two of the patients in this group had definite auditory signs or symptoms. In 16 there was a well-established relationship between the leukemia and the development of these disorders. In an additional 11 there was an almost certain but less definite relationship. There were 6 instances in which an otological complication presented as the only symptom or as part of the initial complaints which brought the patient to the hospital. Four of the 6 patients had acute leukemia. In the others the auditory difficulties developed in the course of the leukemia. In 5 of the 32 patients it was clear that the leukemia was not responsible for the auditory disorders. The most frequent auditory symptoms in the 27 patients were deafness in 16, tinnitus in 7, and pain in 3; only 1 patient complained of vertigo. A few patients were asymptomatic but had bleeding or purulent drainage from an external canal. The term "deafness" is employed to imply varying degrees of hearing loss.

The incidence of otological complications due to leukemia in this small series is 27%. Without the aid of histological examination it was difficult to be sure of the pathophysiology of some of the instances in which acoustic difficulties were encountered. In general, however, patients in whom hemorrhage was responsible usually had acute leukemia. Obstruction of the eustachian canals due to lymphoid hyperplasia was encountered only in chronic lymphocytic leukemia. Infection of the middle ear showed no predisposition to any particular type of leukemia. Auditory difficulties were commoner and developed earlier in patients with acute leukemia than in those with chronic leukemia.

Relief of Deafness by Stapes Mobilization. E. H. M. Foxen. Brit. M. J. **2**:1558-1561 (Dec. 27) 1958 [London].

The author traces the history of stapes mobilization from 1875 when probably Kessel carried out the first mobilization. After a dormant period of half a century the operation was resurrected by Rosen in 1952. Stapes mobilization is most commonly indicated in cases of otosclerosis in which fenestration would have been advised formerly, and it is noteworthy that stapes mobilization is more general in its application than fenestration of the labyrinth. The diagnosis of otosclerosis should be firm and the hearing loss reasonably symmetrical. Pure-tone audiometry should ideally show a 35-to-55-db. loss of air conduction for the critical speech frequencies with a satisfactory air-borne gape (preferably at least 20 db.). Amplification should be well tolerated, paracusia present, and Schwartze's sign absent. Local analgesia is preferred but is not obligatory. After the incudostapedial joint and the surrounding anatomic structures have been displayed, maneuvers aimed at freeing the stapes are carried out. If mobilization is found to be impossible, fenestration of the stapes footplate is undertaken. The progress of the operation is controlled by hearing tests at intervals. Absorbable gelatin sponge (Gelfoam) provides a suitable dressing and may be retained by a strip of ribbon-gauze, which is removed after 2 to 4 days. As a rule, no particular sedation is required, and the patient is usually discharged on the 4th or the 5th postoperative day. Penicillin is given regularly during this time.

A comparison between features of stapes mobilization and fenestration shows that, when such matters as length of stay in the hospital and postoperative discomfort are considered, the magnitude of the former operation is much less than that of the latter. Results to date suggest that, of the patients undergoing stapes mobilization, about 33% may be expected to obtain a useful, lasting, and, in some cases, great hearing improvement; 33%, a slight improvement; and the remainder, no improvement. In a patient in whom the result is disappointing, the fact that the operation may have been performed several times does not preclude him from undergoing fenestration of the labyrinth at a later date.

THERAPEUTICS

Reversal of Intractable Cardiac Edema with Prednisone (Meticorten). D. A. Newman. J. Florida M. A. **45**:778-782 (Jan.) 1959 [Jacksonville].

Ten patients with intractable cardiac edema were subjected to treatment with steroid preparations, principally prednisone. There were 7 men and 3 women, ranging in age from 60 to 85 years. All had arteriosclerotic heart disease, which was associated in 6 with hypertension; 5 of the patients had had myocardial infarction previously. Two patients had aortic regurgitation; 1 had pericardial calcification and constriction; 1 had diabetic glomerulosclerosis with the nephrotic syndrome; 3 had associated bronchopulmonary disease; and 1 had a recognized but quiescent duodenal ulcer. All these patients had been under treatment for congestive heart failure for 2 or more years. Since the standard therapeutic measures had been exhausted, they had become unresponsive to mercurials, to chlorothiazide, to aminophylline, and to such other treatments as induced hyperchloremic acidosis by the combined use of ammonium chloride and Diamox. These patients were considered as calculated risks and were treated accordingly with appropriate countermeasures.

Treatment with corticotropin (ACTH) was attempted in the first of the 10 patients in the series, but it proved a failure. A second patient who was treated with prednisone died after a cerebrovascular accident, but a good remission was obtained with this drug in the remaining 8 patients. The administration of prednisone was started in daily doses of 2.5 mg. This dosage was cautiously increased to between 15 and 20 mg. a day for 4 or 5 days and was then gradually decreased over a varying time interval, depending on each patient's response to the mercurial given after the priming with prednisone. With the onset of diuresis the daily maintenance dose varied from 2.5 to 10 mg. No other change in standard therapy for congestive heart failure was instituted. The intake of water and fluids was neither restricted nor enforced, except in 2 patients with hyponatremia; in the case of these patients a moderate restriction of fluids to 1 or 1.5 liters a day was recommended. Salt restriction was urged to a maximum of 1 Gm. per day. Ammonium chloride was given for one day before, one day during, and one day after the mercurials, when these were given by injection.

The most gratifying feature in the 8 patients who obtained remission with prednisone was the subsequent return of responsiveness to diuretics—not only to injection of mercurials in much smaller doses than previously but also to Diamox, to chlorothiazide, and even to the oral administration of Neohydrin. Diamox seemed to be unusually effective in the patients with additional bronchopulmonary disease and in the one with constrictive pericarditis. Five of the 8 patients have remained in good compensation for periods ranging from 9 to 28 months, but the other 3 have died. The first of these, a 76-year-old man with pericardial constriction and previous myocardial infarction, who had been in excellent compensation for more than 2 years on 2 tablets of Diamox a week and 2.5 to 5 mg. of prednisone a day, died suddenly of pulmonary embolism after he had discontinued this medication in favor of chlorothiazide without prednisone. The second patient died at the age of 74 years of an acute myocardial infarction 9 months after the initially successful reversal of the intractable cardiac failure. The third patient died at the age of 69 years of bronchopneumonia 14 months after a similar successful reversal. The intervening period of maintenance treatment had been most satisfactory as regards both relative comfort to the patient and general ease of management.

Clinical Evaluation of Povidone-Iodine Aerosol Spray in Surgical Practice. A. L. Garnes, E. Davidson, L. E. Taylor and others. Am. J. Surg. **97**:49-53 (Jan.) 1959 [New York].

The authors used the complex of iodine and polyvinylpyrrolidone (povidone-iodine) in the form of an aerosol spray (Betadine Aerosol Spray) as an antiseptic and germicide in the preparation of 200 patients with lacerations for emergency suture, in the preparation of the skin in major surgical interventions on 100 patients, in the treatment of 16 patients with severe burns, and in the treatment of 15 patients with stasis ulcers of the leg. The wounds of all the patients with lacerations healed per primam without side-reactions or evidence of local irritation. Bacteriological cultures taken from the sites before and after operation indicated that all pathogenic agents were eliminated by wiping the skin dry and spraying the Betadine aerosol over an adequate surface; the only remaining organisms were saprophytes and diphtheroids. Biopsy of a skin specimen showed no penetration of the epidermal layers. Although most of the 100 patients subjected to major surgical procedures had established peritonitis or peritonitis due to spillage of intestinal contents, there were no wound infections in this group of patients and all operative incisions healed per primam.

In the patients with second-degree and third-degree burns, treated by spraying with the Betadine aerosol every 12 hours for the first 72 hours and daily thereafter until separation of the eschar began, the medication and method of application facilitated the open therapy of burns, providing a protective covering for areas denuded of skin. The antiseptic properties of the spray controlled infection and inhibited odor. Severely burned children found this form of treatment acceptable. In the patients with stasis ulcers, the lesions were sprayed

twice or three times weekly with the Betadine aerosol, and compression bandages were applied. No side-reactions or satellite ulcers developed. The antiseptic agent aided in the maintenance of an environment ideally suited for healing. Even when it was applied to large, open wounds, discomfort was mild and transitory. Protein-bound iodine determinations did not reveal appreciable change in pretreatment and post-treatment levels. Providone-iodine spray is a safe, time-saving, effective antiseptic and germicide for surgical wounds, burns, and stasis ulcers.

Palliative Chemotherapy of Solid Tumors with Nitromin. R. G. Mrazek and S. G. Economou. A. M. A. Arch. Surg. **78**:51-55 (Jan.) 1959 [Chicago].

The authors report on 48 patients with various advanced malignant tumors who were treated with Nitromin at the tumor clinic of the Research and Educational Hospitals of the University of Illinois in Chicago. An average dose of 402 mg. was given, usually as 50 mg. per day. The drug was administered by the intravenous, intraperitoneal, or intrapleural route. Nitromin is an alkylating agent which was developed during the search for compounds which would have the therapeutic effect of nitrogen mustard with lessened toxicity. Of the 48 patients, 4 had malignant lymphoma, 5 had adenocarcinoma of the stomach, 8 had adenocarcinoma of the colon and rectum, 2 had adenocarcinoma of the pancreas, 4 had tumors of the kidney, 10 had bronchogenic carcinoma, 5 had squamous-cell carcinoma, 4 had malignant melanoma, 1 had carcinoma of the breast, and 5 had miscellaneous tumors. Two of the 4 patients with lymphoma showed reduction in fever and diminution in the size of the spleen and liver. Formation of pleural fluid was reduced in one patient with bronchogenic carcinoma and in one with metastatic adenocarcinoma of the thyroid gland. One patient with adenocarcinoma of the stomach with liver metastases had an improved sense of well-being, an increase in appetite, and relief of pain. These 5 patients obtained relief with relatively small total doses of Nitromin, 200 to 500 mg., whereas as much as 800 mg. was given to the other 43 patients with no effect; 24 of the latter are dead. Side-effects, such as nausea and vomiting, were frequently seen, but severe leukocyte depression was observed only in 3 patients. Nitromin did not cause local irritation or venous thrombosis.

The almost uniformly discouraging results in these patients with far-advanced carcinoma contrast completely with the well-documented demonstration that Nitromin can completely free rats of Yoshida ascites sarcoma implants, if given when the tumors are still small. The authors agree with Ishidate and Druckrey that Nitromin might be effective in patients with tumors in the early stages, or when administered in combination with surgical treatment to destroy microscopic tumor remainders, or when given intravenously after operation to destroy free cells in the blood. Nitromin has the advantages of low toxicity, ease of injection, and relative freedom from side-effects.

Chlorothiazide (Chlotride) in Edema: Clinical Tests with a Mercurial Diuretic. D. Jensen and H. S. Mathisen. Tidsskr. norske lægefor **78**:1166-1170 (Dec. 1) 1958 (In Norwegian) [Oslo].

Twenty-eight patients (average age, 68½ years) were treated with chlorothiazide for from 3 to 9 days because of edema. In all, 61 treatments were given. The chlorothiazide dose was usually 0.50 Gm. daily, i. e., ½ tablet twice daily, preferably in the morning and at noon; in 5 tests 1 Gm. was given daily, in 2 cases the dose was reduced to 0.25 Gm. daily. The average increase in diuresis was about 70% daily; the average loss of weight during the time of treatment was 0.31 kg. (¾ lb.) daily. The maximal increase in diuresis averaged 143%, with variations between 29 and 323% in the different periods of treatment. The authors found that chlorothiazide seems to approach the ideal diuretic. It was in several tests equal to or superior to mersalyl and better than other diuretics tried for oral use. With the dosage applied, the agent was practically free from side-effects.

Pathological and Biochemical Considerations on Chronic Alcoholism with Relationship to the Therapeutic Effect of Liver Extracts Administered Intravenously. P. Benassi and D. Munarini. Minerva med. **49**:4334-4341 (Nov. 24) 1958 (In Italian) [Turin, Italy].

Intravenous administration of Ripason, an Italian proprietary liver-extract preparation, had a beneficial effect on 30 chronic alcoholic patients. Before the treatment the tolerance of each patient was tested by parenteral administration of 1 cc. of this liver extract; during treatment the patient received a daily dose of 3 or 4 cc. The preparation was always introduced into the vein with some rapidity. Twenty patients were treated for 30 days and 10 patients for 60. The drug was well tolerated and did not cause undesirable side-effects during or after its injection. Clinically, an improvement, at times very marked, of the general condition and of the metabolism followed in all the patients; the appetite increased and the cenesthesia improved markedly. Psychologically, the preparation had a beneficial antidepressive effect on the adjustment of the patients to the environment, and caused improvement in their daily work and general behavior. The group of patients who received treatment for 2 consecutive months showed improvement in the Takata, Wuhrman-Wunderly, and Kunkel laboratory tests.

A New Treatment for Cutaneous Larva Migrans: Employing Oral Promethazine. J. L. Greene. J. Florida M. A. **45**:784-788 (Jan.) 1959 [Jacksonville].

The oral administration of promethazine (Phenergan) hydrochloride to 57 patients with creeping eruption caused by larva migrans is reported. The group included both sexes and ranged in age from 14 months to 68 years. The patients presented skin lesions on various parts of the body, but the extremities, the back, and the perineum were more frequently involved. The compound was administered at bedtime—as a sirup to children up to the age of 6 years in doses of 50 mg. and as tablets to older children in doses of from 75 to 100 mg.; adults were given oral doses of 150 mg. or more. The same doses were given on 3 successive nights, and occasionally it was necessary to repeat the course with the same amount or with an increased dosage.

The oral administration of promethazine was a failure in the first 6 patients (10.5%) who were given only small doses (25 mg.) of the drug. The pruritus, however, promptly disappeared in all the remaining patients (89.5%) after the first larger doses of promethazine were given; at the same time the marked redness and the prominence of the skin lesions began to fade, and healing was complete within 3 or 4 days. The soporific properties of promethazine, which are entirely separate from the activity of the compound upon the larva, were an advantage to these patients, since insomnia caused by intense itching is one of the consequences of cutaneous larval infestation. The hyperexcitability exhibited by some patients after the ingestion of the first dose of this compound may be promptly controlled by an additional dose, and this reaction does not represent a contraindication to the use of the compound. The success obtained solely by the oral administration of promethazine is of great interest, since all treatments so far suggested for cutaneous larva migrans have been disappointing.

Absorption of Orally Administered Vitamin B_{12} in Pernicious Anaemia. J. N. M. Chalmers and N. K. Shinton. Lancet **2**:1298-1302 (Dec. 20) 1958 [London].

Fifteen men and 6 women, between the ages of 43 and 82 years, with pernicious anemia in relapse were treated for 15 days with daily doses of vitamin B_{12} given orally alone. The amount of vitamin B_{12} given ranged from 20 to 500 mcg. daily. The larger the daily dose of vitamin B_{12} given orally, the more prompt was the hematological response and the return of the serum vitamin B_{12} level to the normal range. Long-term maintenance therapy with daily doses of vitamin B_{12} was given orally to 12 patients, 3 of whom received doses of 50 mcg. daily for periods ranging from 21 to 50 months, 3 received doses of 100 mcg., 2 received doses of 200 mcg., and 4 received doses of 500 mcg. daily for periods ranging from 6 to 26 months. Results showed that daily doses of 100 mcg. or more of vitamin B_{12} given orally can be effective in maintenance therapy. These findings provide further proof that vitamin B_{12} given orally can be absorbed and utilized by patients with pernicious anemia. Some of the patients obtained normal hematological values and clinical remissions without return of serum vitamin B_{12} level to normal. Parenteral therapy with vitamin B_{12} is still the most reliable method of ensuring freedom from relapse in pernicious anemia, but with the close cooperation of the patient oral treatment by daily application may be effective.

Vitamin B_{12} in Pernicious Anemia: Intramuscular or Oral? E. H. Hemsted and J. Mills. Lancet **2**:1302-1303 (Dec. 20) 1958 [London].

The authors compared the effects of oral and intramuscular administration of vitamin B_{12} in patients with pernicious anemia treated at the Royal Berkshire Hospital in Reading, England. Over a period of 2 years a group of 71 patients taking a daily dose of 100 mcg. by mouth one hour before breakfast were maintained at least as well as a group of 84 patients receiving a monthly intramuscular injection of 100 mcg. Thirty-four patients with pernicious anemia were treated for 2 years with intramuscular injections of 1,000 mcg. of vitamin B_{12} per month; there was no significant change in hemoglobin and red blood cell levels, and, therefore, no advantage in a higher dose than 100 mcg. per month for maintenance treatment was apparent.

PATHOLOGY

Coccidioidal Pulmonary Cavitation. L. Hyde. Am. J. Med. **25**:890-897 (Dec.) 1958 [New York].

The author reports on 76 men and 1 woman with coccidioidal pulmonary cavitation, 57 of whom were studied at the Veterans Administration Hospital in Long Beach, Calif., and 20 were included in the Veterans Administration–Armed Forces Cooperative Study of Coccidioidomycosis. The median age was 25 years; 90% were under 40 years of age. Coccidioidal pulmonary cavitation occurred in 2 or 3% of those patients in whom primary infection due to Coccidioides immitis was severe enough to cause consultation of a physician. Fifty-eight per cent of the whole group were essentially asymptomatic, and the condition was detected on the taking of routine chest roentgenograms; 26% were subjected to roentgenography because of hemoptysis, 6% because of chest pain, and 10% because of acute respiratory symptoms. In most of the patients who gave a history of bleeding, there had been only minimal blood streaking or a small hemoptysis. Cavitation in this disease occurs at the site of the

original coccidioidal pneumonia. Generally there are no signs or symptoms during the process of cavitation in hospitalized patients. Eighty-six per cent of the 77 patients in this series had a single cavity, and 14% had multiple cavities. Fifty-eight per cent of the cavities were in the right lung, and 42% in the left lung; 3 patients had bilateral cavities. The results of the coccidioidin skin test were positive in 57% of the 73 patients for whom the results were recorded. In most cases the skin test was made once, but for some it was repeated on numerous occasions. Sixty-four per cent of the 77 patients had positive complement-fixation antibodies in varying degrees.

Nonsurgical and surgical treatment in patients with coccidioidal pulmonary cavitation has been compared. Forty-six per cent of the whole group were treated nonsurgically. Most patients were asymptomatic, but 22% of this group had a history of bleeding; no new cavities developed in any of the 36 patients. Fifty-four per cent of the 77 patients underwent resectional surgery. Twenty-nine of these patients were asymptomatic, although 30% gave a history of bleeding. There were no deaths, but in 29% of the patients who had resection, bronchopleural fistulas with empyema developed, and 20 additional surgical procedures were required. Furthermore, new cavities appeared postoperatively in 20% of the patients who underwent resection. On the basis of these findings a conservative nonsurgical treatment appears most desirable for patients with coccidioidal pulmonary cavitation, unless the cavity is more than 4 cm. in diameter or is enlarging significantly or there have been recurrences of severe hemoptysis.

Incidence and Prognosis in Cancer of the Rectum in a Danish Provincial Town. N. Blixenkrone-Møller. Danish M. Bull. 5:268-272 (Dec.) 1958 (In English) [Copenhagen].

From 1946 to 1955, 180 cases of rectal cancer, in 112 men and 68 women, were diagnosed in Aarhus (population of about 113,000). In all but 10 cases the diagnosis was confirmed by histological examination; in 6 of the 10 there were metastases, and 4 were clinically unquestionable. Most cases occurred between the ages of 60 and 70 years. Up to the age of 60, cancer of the rectum is equally frequent in men and women; a steep rise then occurs among men. The lower margin of all tumors was at a level of 20 cm. or less from the anus at proctoscopic examination. Of the 170 cases examined histologically, 158 were adenocarcinomas; 6, solid carcinomas; 5, malignant papillomas, with typical invasive growth; and 1, a lymphosarcoma. Diagnosis was made within the first 3 months after the onset of the first symptom in only 42% of the cases. About 30% of the cases were radically inoperable. Major radical operation was performed on 98 of the patients with radically operable cancer. Of these, 37% were living 5 years later, or, corrected for deaths from unrelated causes, 43%. Of the entire group of 180 patients, only 20% were living after 5 years. A few had died of causes other than cancer. The prognosis is better for the age group under 60. There was no demonstrable difference in the prognosis for men and for women. The analysis shows that removal of skin and pelvic connective tissue must be more radical.

Fat Embolism in Chronic Alcoholism: Control Study on Incidence of Fat Embolism. M. J. G. Lynch, S. S. Raphael and T. P. Dixon. A. M. A. Arch. Path. 67:68-80 (Jan.) 1959 [Chicago].

The changes found in the central nervous system in association with chronic alcoholism appear to be ill-defined. Wernicke's "superior hemorrhagic polioencephalitis" was specifically linked to chronic alcoholism, and Gudden's atrophy of the corpora mammillaria was somewhat later similarly associated; however, subsequent observations cast much doubt on the specificity of the association between the Wernicke-Gudden changes and alcohol addiction. It is now accepted that the lesions described by these pioneers are due to concomitant vitamin deficiencies. Although general dietary improvement has altered the neuropathological picture of chronic alcoholism, certain diffuse or patchy, ill-defined, and apparently nonspecific changes, such as loss of neurons, focal degenerative lesions, atrophy, and astrocytic proliferation, remain to be explained.

The interest of the present authors in this problem was aroused by the work of Hartroft and Ridout, who demonstrated that in rats fed on choline-deficient diets "fat cysts" develop in the livers and that such large fat globules may rupture into biliary or vascular channels. These workers examined human autopsy material from 30 cases of chronic alcoholism and found "small amounts of embolic fat within the vessels of the lungs and kidneys in a number of cases." In preliminary studies on 250 consecutive autopsies, the present authors found fat embolism only in cases of trauma, alcoholic fatty liver, and necrotizing pancreatitis. However, in that series only one block each from lung and kidney was examined, and these were not uniformly selected as to size or site. For the present investigation a more thorough study was planned, and a block from each lung was selected and examined.

From the beginning of 1957 to the present time the authors have made studies on 51 patients with alcoholic psychosis admitted to their psychiatric unit. Morning sputum samples were examined for fat droplets, which were found in 48 of them. The 3 patients with sputums which were negative for fat globules had little more than "hangovers." The authors conclude that fat embolism is of common

occurrence in chronic alcoholics. Fat embolism is advanced as a major factor in the etiology of alcoholic psychoses and may lead to death in some such cases. Repeated fat embolism may be the basis of some, at least, of the changes noted in the brains of chronic alcoholics.

Rheumatic Pneumonitis: Pathological Features. R. F. Scott, W. A. Thomas and J. M. Kissane. J. Pediat. **54**:60-67 (Jan.) 1959 [St. Louis].

Autopsy was performed on 87 children, ranging in age from 3 to 16 years, who died of pneumonitis due to rheumatic fever during 1919-1954 at the St. Louis Children's Hospital. Microsections of the lungs were examined especially for fibrinous exudate in the alveolar sacs or respiratory ducts, hyaline-like membrane, and necrosis of the alveolar walls and thrombi. Pathological changes were graded as "slight" if less than 10% of the tissue available for miscroscopic study was estimated to be involved, "moderate" if 10 to 20%, and "advanced" if more than 20%. With this criterion, 21 cases (39%) showed slight pathological change; 29 (54%), moderate change; and 4 (7%), advanced change. The cases were divided into 3 age groups—3 to 5 years, 6 to 10 years, and 11 to 16 years. The incidence of rheumatic pneumonitis in each group was as follows: 8 of 11 cases (73%) in the youngest group; 24 of 32 cases (75%) in the intermediate group; and 24 of 44 cases (55%) in the eldest group. Gross findings were not distinctive. Most anatomic specimens revealed only congestion and edema; only occasionally were there grayish-red and firm lungs which exuded little fluid and were suggestive of rheumatic pneumonitis. Histologically, the most characteristic feature was a patchy, dense, fibrinous exudate in the alveolar sacs and in the respiratory ducts. This exudate was in the form of irregular globular masses or membranes and was almost invariably associated with monocytes (many containing hemosiderin) and protein-rich edema fluid. Intra-alveolar hemorrhage was common. No consistent difference was found between the anatomic features -seen in pneumonitis due to rheumatic fever and those in pneumonia associated with other diseases.

Histomorphologic Study of the Changes of Arterial Walls from Birth Until the Age of Twenty, with Particular Reference to the Coronary Arteries. M. Bisiani. Minerva cardioangiol. **6**:519-536 (Oct.) 1958 (In Italian) [Turin, Italy].

Histological examination of the walls of the sylvian arteries, of the aorta, of the anterior descending coronary artery, and of a section of renal arteries was made in 56 patients. There were 33 males and 23 females, aged between birth and 20 years. These patients had died of an acute disease, such as acute enterocolitis or acute appendicitis, and none of them had a posthumously observed lesion of a more remote disease. Histological changes and the rate of thickening with age of the aorta and of the sylvian and renal arteries in these patients were gradual and similar, whereas those of the coronary arteries were dissimilar to the changes observed by other workers. The structure of the intima of the coronary arteries started to change after a few weeks of life, while the tunica media and the adventitia appeared normal. At the age of 3 or 4 months a sectional thickening of the subendothelial connective tissue of the coronary arteries was observed in both sexes. Various processes took place in the intima, involving edematous imbibition of the subendothelial mesenchyma, neoformation of elastic fibers, thickening and splitting of internal elastic membranes, and formation of fibroblastic cells, histiocytes, and lymphoids. Endothelial cells also seemed to participate in these precocious changes, exhibiting mild regressive processes. The intima thickened, and gradually larger sections of it became affected with age. After the first decade of life, thickening of the subendothelial mesenchyma involved the whole intima, which was in some sections thicker than the tunica media. The hyperplastic process apparently did not affect the tunica media and only slightly the adventitia. Lipids started to appear when thickening of the intima reached or surpassed that of the tunica media.

Pseudomonas Septicemia: Observations on Twenty-three Cases. C. E. Forkner Jr., E. Frei, J. H. Edgcomb and J. P. Utz. Am. J. Med. **25**:877-889 (Dec.) 1958 [New York].

The authors report on 23 patients with malignant neoplastic disease (13 of these patients had acute leukemia, 1 had acute disseminated histoplasmosis, and 1 had mycosis fungoides). In addition, these patients, who were seen at the clinical center of the National Institutes of Health in Bethesda, Md., between 1954 and 1957, had the complication of septicemia due to Pseudomonas organisms. The common clinical manifestations of Pseudomonas septicemia include characteristic cutaneous lesions, progressive jaundice, neurological abnormalities, arrhythmia, ileus, and sudden development of hypotension. Twenty-two of the 23 cases were fatal. The median duration of life after identification of the first positive blood culture was 4 days. The most striking gross and morphologic changes were the cutaneous lesions, which were classified according to the following 4 categories: (1) ecthyma gangrenosum, which mostly occurred in the anogenital area; (2) vesicular lesions, which tended to occur in clusters; (3) flat and sharply demarcated cellulitis, which after rapid enlargement became hemorrhagic and necrotic; and (4) small, pink, round maculopapular plaques or nodules, characteristically found

on the trunk. In the course of Pseudomonas septicemia metastatic abscesses may appear in any part of the body. The affinity of Pseudomonas organisms for the walls of small vessels is stressed.

Of the 23 patients in this series, the 13 with acute leukemia were selected, as a group, for the analysis of epidemiology and host resistance. Pseudomonas aeruginosa was the second most frequent cause of septicemia and the most frequent bacterial cause of death on the acute leukemia service. The cases of Pseudomonas septicemia on the acute leukemia service were noted to occur in groups, in contrast to the random distribution of other bacterial septicemias occurring on that service. Gram-negative septicemias occurred more frequently than septicemias due to gram-positive bacteria in patients receiving adrenal steroid therapy. Of the 13 incidences of Pseudomonas septicemia, 10 occurred in patients receiving broad-spectrum antimicrobial therapy, whereas the respective figure for other gram-negative septicemias was only 12 of 22 incidences, and for gram-positive infections only 13 of 39 incidences. These data add to the evidence that Ps. aeruginosa is a common super-infecting organism. There is suggestive evidence that antimetabolite administration may in some way predispose to the development of Pseudomonas septicemia.

Familial True Hermaphrodism in Pre- and Postpuberal Genetic Females: Hormonal and Morphologic Studies. G. W. Clayton, J. D. Smith and H. S. Rosenberg. J. Clin. Endocrinol. **18**:1349-1358 (Dec.) 1958 [Springfield, Ill.].

Two siblings with scrotal testes and ovaries are presented. The first, aged 16 years, except for a congenital abnormality of the penis described as "complete hypospadias without cryptorchidism," which had been successfully repaired at age 4, appeared to be a psychologically well-orientated male. Concomitant with the normal puberal changes —growth spurt, increase in size of the penis, appearance of sexual hair, and deepening of the voice, there had been progressive enlargement of the breasts. In retrospect the testes were noted to have remained small and insensitive. The family history was significant in that a 7-year-old brother had a similar congenital abnormality of the external genitalia. A 12-year-old brother was normal. A smear of the buccal mucosa in the 16-year-old sibling demonstrated a positive nuclear chromatic pattern, but urethrograms failed to reveal vestiges of the Müllerian system. Hormonal studies showed a low urinary excretion of 17-ketosteroids, an elevated excretion of estrogens and pregnanediol, and a normal excretion of gonadotropins. The initial impression was Klinefelter's syndrome; however, the familial hypospadias suggested that a more complex type of gonadal dysgenesis existed.

The second sibling, now aged 7 years, had been born prematurely. The infant had been considered normal except for a defect in the external genitalia. A phallus of normal size was bound down ventrally and lacked a urethral meatus. Urine was emitted through a small opening at the base of the phallus. The normal-appearing scrotum contained palpable gonads. An abdominal exploration carried out in infancy revealed no female internal genitalia. The construction of a penile urethra was completed at the age of 6 years. At 7 years the boy was of normal height and weight. The penis was slightly hooded at the base with a fold of skin, but otherwise appeared normal except for old operative scars on the ventral surface. The scrotum contained small, very mobile gonads of normal consistency. This child also had a positive nuclear chromatin pattern in the buccal smears, and a urethrogram showed that there were no Müllerian vestiges. Studies of urine samples revealed a normal excretion of 17-ketosteroids and estrogens, a slightly elevated excretion of pregnanediol, and a gonadotropin excretion of less than 6 mouse units.

The scrotal contents were explored in both siblings. The testes of the postpuberal sibling showed seminiferous tubule dysgenesis which was identical to that found in Klinefelter's syndrome, whereas the testes of the prepuberal sibling were histologically normal. Sections of the 1-cm. oval mass from the upper pole of the right testis in the first sibling revealed ovarian tissue, consisting almost entirely of stromal elements in which a few scattered primordial and atretic follicles were identified. In the epididymis there was a tubular structure, lined by a pseudostratified columnar ciliated epithelium; this structure was presumably a vestigial fallopian tube. In the 7-year-old sibling a section of ovary sat cap-like on each testis. Within the ovary there was abundant stroma with numerous peripherally placed primordial follicles. Peripheral clumping of nuclear chromatin, characteristic of the female, was demonstrable in many Leydig cells in the testes of the first sibling and in the seminiferous tubule cells of the second sibling. As far as the authors know, this is the first reported instance of familial true hermaphrodism. In an addendum they call attention to a recent report on 2 siblings with true hermaphrodism in whom the chromatin pattern was negative.

Further Observations on Infection with Phage Type 80 Staphylococci in Australia. P. M. Rountree and M. A. Beard. M. J. Australia **2**:789-795 (Dec. 13) 1958 [Sydney].

In 1953 a new phage type of Staphylococcus pyogenes var. aureus was isolated from infections of newborn infants in a Sydney maternity hospital. Later it was found that this particular strain, which had been given the phage type designation 80, had

been responsible for a large proportion of outbreaks of neonatal infection in hospitals throughout Australia during 1954, and that it had become established as a cause of cross infection in adult patients at the Royal Prince Alfred Hospital, Sydney, where it had also caused an epidemic of boils in the staff. In 1955 and 1956 investigators found that the majority of penicillin-resistant staphylococci isolated from boils in Sydney belonged to this type. Apparently the same type of Staphylococcus organism was observed in Canada, and it was identified with phage type 81. The 2 phages, 80 and 81, are not identical, but their propagating strains are lysed by both phages and can be regarded as identical; their typing pattern is, therefore, 80/81. Other strains occur which are lysed only by phage 80 or only by phage 81, but these are much rarer. Strains of phage pattern 80/81 have been isolated in many parts of the world and have been responsible for much serious staphylococcic sepsis.

The authors report their observations during the 3 years that have elapsed since their first report. The data presented in this paper justify the view that much of the morbidity due to Staph. aureus occurring in Australia in the past 4 years has been caused by strains of phage type 80/81. Staphylococci of this phage type were responsible for 70 of 86 major outbreaks of staphylococcic infection among newborn infants in Australia from 1954 to the end of 1957. They predominated in serious infections in infants and older children admitted to children's hospitals in Sydney. At the Royal Prince Alfred Hospital since 1955 they have been the predominant, but not the only, staphylococci found in cross infection in patients, and they have been the chief cause of staphylococcic lesions in the nursing and medical staffs. Strains of this type are now widespread in communities outside the hospitals. A marked increase in the incidence of generalized staphylococcic infection in 1956 and 1957 was due almost entirely to them. In 9 out of 12 cases of fulminating staphylococcic pneumonia associated with Asian influenza in 1957, strains of this type were the infecting organisms. Nearly all the strains of this type are penicillin resistant, but so far resistance to other antibodies is more limited in extent.

Reaction of Lupus Erythematosus Serum with Nuclei of Circulating and Non-Circulating Cells. W. R. M. Alexander and J. J. R. Duthie. Brit. M. J. **2**:1565-1566 (Dec. 27) 1958 [London].

Experiments carried out by other workers showed that tissue cells brought in contact with serum obtained from patients with disseminated lupus erythematosus and exposed subsequently to fluorescein-conjugated anti-human-globulin (Coombs's) serum showed specific nuclear fluorescence, thus providing strong evidence for the belief that the serum of patients with disseminated lupus erythematosus contains a globulin which combines with nuclei of tissue cells and leukocytes. The authors studied the serums obtained from 8 patients with disseminated lupus erythematosus and observed that nuclei of leukocytes from healthy persons showed the greatest affinity for the specific globulin. No evidence of uptake of globulin in tissue from patients with disseminated lupus erythematosus was found in vivo, but in vitro such tissue had less affinity for the specific globulin than tissue from healthy subjects. Nuclei of intact squamous epithelial cells pretreated with serum obtained from the patients with disseminated lupus erythematosus did not fluoresce on exposure to fluorescein-conjugated anti-human-globulin serum.

Cultivation of Human Breast Carcinomas. E. Y. Lasfargues and L. Ozzello. J. Nat. Cancer Inst. **21**:1131-1148 (Dec.) 1958 [Washington, D. C.].

Although most of the human carcinomas have been successfully transplanted in vitro, the mammary carcinoma has remained a challenge for the investigator. The authors discuss some of the technical difficulties encountered in earlier reported attempts at explantation and growth of neoplastic tissues from human breasts. Recent progress in research on the mouse mammary carcinomas makes it imperative to grow human breast tumors for comparative studies. Since viral induction of these neoplasms in the mouse has gained more support, the availability of human tissue-culture material for experimental purposes could be enlightening, and valuable information might be obtained from its use in screening techniques for therapeutic agents.

The authors have developed a technique for the cultivation of human breast carcinoma cells, which in taking advantage of the weak intercellular bonds within the tumor harvests the cells "spilling" out of the tumor stroma when thin slices are cut with a razor blade. This suspension is sensitive to customary enzymatic concentrations which, therefore, cannot be used in the preliminary step of preparation. Agitation, even the slow motion of the roller drum, is unfavorable to the growth of the neoplastic cells; they have to be explanted in resting tubes.

Continuous cultivation of human breast carcinoma cells has thus been achieved for the first time. The cultures, derived from a mammary-duct-cell carcinoma of no special type, are now in their 6th month of life in vitro and are extremely proliferative. The regular growth rate of the neoplastic cells appears to be dependent on the presence in the medium of mucopolysaccharides introduced in the form of umbilical cord extract. Human placental serum and beef amniotic fluid, whose high content in estrogenic hormones is well known, also have a beneficial effect. Folic acid in a 2.5 mM.

concentration appears favorable to the growth of the cancer cells. However, a possible antagonism with cord extract has been considered in the spindle-shaped transformation which occurs in the epithelial cells when transferred from a folic acid medium to one enriched with umbilical cord extract.

The authors feel that the above-mentioned changes should be kept in mind in relation to the spindle-cell type of carcinomas occasionally observed by pathologists and to the spontaneous sarcomatous transformations of experimental carcinomas reported in the current literature. In an addendum they state that the fibroblast-like cells have again reverted to their original epithelial morphology. Such modifications, therefore, are determined by variations in the environmental factors and are reversible.

RADIOLOGY

Roentgenographic Study of the Progress of Osseous Metastases of Mammary Carcinoma After Bilateral Ovarioadrenalectomy. A. M. Dogliotti, A. Ruffo, F. Badellino and others. Minerva chir. **13**:1213-1225 (Oct. 31) 1958 (In Italian) [Turin, Italy].

The authors report on roentgenologic findings of osseous metastases in 10 patients who underwent a bilateral ovarioadrenalectomy because of mammary carcinoma in an advanced phase. Eight patients died within a period of from 5 to 30 months after the operation. Improvement or deterioration of osseous metastases after operation was more tardily observed by roentgenograms than by clinical means. Cortisone therapy produced improvement in subjective symptoms and in state of health in only a few patients, although roentgenograms demonstrated severe lesions of osseous metastases. Roentgenograms and clinical findings may be dissimilar at particular periods of observation in these patients after operation, but the 2 methods complement each other in the over-all picture. Pictures of osteolytic foci and zones of recalcification, representing simultaneous processes of both bone destructive activities and of reossification, were observed in several patients. Clinical and biochemical findings determined which one of the 2 processes predominated. Periodic roentgenologic inspections of the whole skeleton can be used as a collateral, although tardy, procedure in evaluating the efficacy of bilateral ovarioadrenalectomy in patients with advanced mammary carcinoma. Laboratory investigation of calcemia and phosphatemia was a third procedure used in this series of patients. It can be particularly useful in discovering osseous metastases in those instances in which clinical and roentgenologic findings are negative. Simultaneous application of clinical, roentgenographic, and laboratory investigations seems to be the best method for observing the progress of osseous metastases in patients who have undergone bilateral ovarioadrenalectomy for advanced mammary carcinoma.

Thyroid Cancer in Youth. D. W. Petit, B. Catz and P. Starr. California Med. **89**:394-396 (Dec.) 1958 [San Francisco].

The authors report on 9 boys and 2 girls with cancer of the thyroid, whose ages ranged from 5 to 18 years at the time the diagnosis was made. In 8 of the 11 patients the diagnosis was suggested by persistent enlargement of the cervical lymph nodes. Seven patients were subjected to total thyroidectomy, 3 underwent hemithyroidectomy, and 1 had repeated removal of lymph nodes in the neck, only one of which was cancerous. After total ablation of normal thyroid tissue and removal of as much malignant tissue as possible surgically, scintigram and/or radioautograph studies with radioiodine (I^{131}), administered in doses of 1/10th to 10 mc., were carried out in 9 of the 11 patients. In 6 of the 9 patients uptake of the radioactive material was demonstrated. These 6 patients then were treated with I^{131}, a dose of 100 mc. being given by mouth. Administration of the radioactive agent was continued, with interval studies in which millicurie doses were used for tracer purposes only until no further uptake was observed. During this whole period the patients were kept in a euthyroid state by the administration of thyroid hormone or levothyroxine. The patients were followed up for periods ranging from 10 months to 9 years. Of the 11 patients, 9 were free of metastases as nearly as could be determined. One patient had metastatic pulmonary lesions that were not shown to take up I^{131} and that progressed despite the administration of a total dose of 250 mc. of I^{131}. Another patient had questionable pulmonary metastasis.

Nine of the 11 patients had had roentgenotherapy to the head or neck previous to the diagnosis of thyroid cancer. Other workers had reached the tentative conclusion that irradiation is possibly carcinogenic to the normal preadolescent when given in therapeutic amounts. In 2 previously reported series of thyroid cancer in children, 10 of 28 patients in one and 15 of 15 patients in the other had had roentgen-ray treatment to the head and neck before the cancer was diagnosed. As yet, there have been no surveys that would establish the incidence of head-and-neck irradiation in a population of the kind represented by the authors' patients, but the significance of the reported observations would depend on the incidence. Inasmuch as the ultimate answer to the problem of such irradiation as a possible stimulus to the production of thyroid cancer is not yet at hand, it would seem prudent to avoid, if possible, therapeutic irradiation to the head and neck of preadolescent children with a normal thyroid gland.

Operative Cholangiography in the Diagnosis of Prolonged Jaundice in Infancy. J. H. Harris Jr., A. E. O'Hara and C. E. Koop. Radiology **71**:806-815 (Dec.) 1958 [Syracuse, N. Y.].

Whereas in many institutions operative cholangiography is a routine procedure during biliary tract surgery in adult patients, the value of delineating the biliary ductal system in pediatric surgery is not generally realized. The authors describe the technique of operative cholangiography that is being used at the Children's Hospital of Philadelphia. The peritoneal cavity is entered through a small right subcostal incision, and the gallbladder is identified. If the latter is of normal size and contains normal appearing bile, a patent communication between the gallbladder and the liver may be assumed, but this does not reflect the caliber of the communication. Furthermore, this does not aid in the differentiation between the "inspissated bile syndrome," viral hepatitis, and atresia of the common bile duct. A mushroom catheter is inserted into the gallbladder through a small cholecystostomy, and held in place with a purse-string suture. After irirgation of the biliary ductal system to eliminate artefacts caused by bile plugs, 8 to 20 cc. of 15% Urokon is injected through the catheter. It is important that the patient be apneic during the x-ray exposure, and that the exposure be made after approximately 80 to 85% of the contrast medium has been introduced. The authors attempt to obtain a right posterior oblique projection in order to avoid superimposition of the ductal structures and to project them away from the spinal column. If the cholangiographic findings indicate a normal biliary ductal system with free flow of the contrast medium into the duodenum, a liver specimen is taken for biopsy, and the abdomen is closed. If, on the other hand, there is roentgenologic evidence of atresia of the ductal system, the initial incision is extended to allow adequate exposure for exploration of the porta of the liver.

Since 1953 operative cholangiography has been employed in 12 instances. Three infants were 1 month of age; the oldest child was 21 months old. Of the 12 patients, 6 were found to have normal extrahepatic ductal systems, 1 had atresia of the common bile duct, and 4 had congenital atresia of the hepatic ducts. The histories of 4 of the children are described in detail. In one of these no contrast medium was seen in the common hepatic duct or its radicals, and the roentgenogram was interpreted as representing atresia of this portion of the ductal system. However, when the cholecystostomy was done, normal bile was found in the gallbladder, and because of this the roentgenologic findings were considered to be falsely indicative of biliary atresia. The liver biopsy specimen, taken at the time of laparotomy, revealed hepatitis. In each of the other 11 cases, the operative cholangiographic findings helped the surgeon. When a normal biliary tree was outlined, the abdomen was closed. The surgical procedure was thereby shortened, reducing both the surgical trauma and the exposure of the already embarrassed liver to anesthetic agents. In addition, since only the gallbladder was involved in the surgical dissection, the possibility of postoperative fibrosis about the normal infantile ducts was avoided.

The causes of jaundice in newborn and older infants are icterus neonatorum, congenital hemolytic jaundice, erythroblastosis fetalis, syphilitic hepatitis, jaundice due to sepsis, intrauterine viral hepatitis, and congenital atresia of the bile ducts. Uncorrected atresia of the bile ducts is not compatible with long life, although many patients survive for some years. The early clinical picture is that of a jaundiced child with dark urine and acholic stools. Recent work tends to implicate the virus of homologous serum hepatitis in acquired biliary atresia. The fact that biliary atresia is the most frequent cause of obstructive jaundice in infancy, that in its unaltered course the disease is fatal, and that only early surgical correction can prevent the cirrhotic process emphasizes the importance of early limited exploration and study of the biliary ductal system by operative cholangiography.

Undulant Fever Spondylitis. F. Zammit. Brit. J. Radiol. **31**:683-690 (Dec.) 1958 [London].

Undulant fever caused by Brucella melitensis is endemic in Malta and causes much disability. Diagnosis is difficult during its early stages. The blood should be tested for the agglutination reaction. A serum agglutination reaction of 1:80 is regarded as diagnostic, but in some cases the reaction does not rise above 1:40. A rising titer is indicative of active brucellosis. Blood culture is not always positive. Bone marrow examination may help in the diagnosis, especially when it is drawn from the sites which show roentgenologic signs of bone involvement. The main symptom of this disease is a highly irregular fever, with the temperature rising and falling, which goes on for long periods and is often associated with headaches, enlargement of the spleen, excessive perspiration, secondary anemia, weakness, and pains of a rheumatic type. The commonest sites of these rheumatic pains are the neck, shoulder, lumbar region, hip, thigh, and knees.

The author reviewed all the cases diagnosed as brucellar spondylitis in the orthopedic department of a hospital in Malta from 1947 to 1954. During this period spondylitis was diagnosed in 115 of 6,301 patients with undulant fever. In a typical case the signs and symptoms of spondylitis manifested themselves during the period of convalescence from brucellosis. The earliest and most

constant symptom was pain, localized to the affected region of the spine. It was made worse by movements and was relieved by rest. Referred pains to the limbs, and in some cases the girdle type, occurred. Spasm of the spinal muscles was commonly present. In 62 of the patients roentgenologic evidence of spine involvement was found; the regional distribution was as follows: cervical, 5; thoracic, 16; combined thoracic and lumbar, 4; and lumbar, 37. The 4th lumbar vertebra was most commonly involved. The main changes were destructive lesions in the vertebral bodies, usually marginal, with characteristic sclerotic reactions around them and proliferative marginal new bone formations resembling calcifications of ligaments or osteophytic processes. The disk space was usually narrowed. Signs of cord compression were present in 8 patients. The following conditions have to be differentiated from brucellar spondylitis: Pott's disease, staphylococcic osteomylitis, actinomycosis, osteochondrosis of the vertebrae, and osteoarthritis.

Treatment is largely conservative; in recent years antibiotics have been administered with favorable results. The author found that most patients derived benefit from rest in bed or on a Bradford frame. When root pains, with radiation to the upper and lower limbs, were present, traction was applied, and the patient was eventually relieved. When the condition of the patient improved and the pain abated or disappeared, a plaster jacket was applied. Recovery took place after several months, depending on the extent of the lesion, and in the majority of cases the patient returned to his former work. The period of disability varied from 3 to 6 months in 60% of the patients; in the rest, in whom the lesion was more extensive, it lasted longer.

PUBLIC HEALTH

Effect of Ingestion of Distilled Spirits on Automobile Driving Skill. B. B. Coldwell, D. W. Penner, H. W. Smith and others. Quart. J. Stud. Alcohol 19:590-616 (Dec.) 1958 [New Haven, Conn.]

The authors carried out practical road tests on 50 experienced automobile drivers who consumed known amounts of distilled spirits. Under the given experimental conditions, the impairment of driving skill was definitely evident in one subject in whom the venous blood alcohol level was 0.036%. Signs of impairment were observed in 5 out of 7 subjects whose venous blood alcohol levels at the time of driving did not exceed 0.05%. Heavy drinkers showed less impairment of driving performance than light drinkers with the same blood alcohol levels, but signs of impaired driving ability were exhibited by 8 out of 10 heavy drinkers with venous blood alcohol levels ranging from 0.051 to 0.12%. Not one subject in whom the blood alcohol level was around 0.15% was able to maintain his driving ability as shown before drinking. Twenty-five drivers manifested significant impairment of their driving abilities when their venous blood alcohol level was 0.078%. The impaired ability in handling cars, such as manipulation of clutch, brake, gearshift, and accelerator, even at a relatively low venous blood alcohol level, was the most striking feature in the tests, in contrast to the drivers' skill to avoid stanchions. The experimental driving situation favored the subjects; therefore, one may assume that the influence of alcohol would be more pronounced on the driving performance in urban areas than on that observed in the tests.

Vaccination Against Poliomyelitis with Living Avirulent Viruses: Preliminary Report. F. Buser and M. Schär. Schweiz, med. Wchnschr. 88:1282-1284 (Dec. 20) 1958 (In German) [Basel, Switzerland].

Killed or living viruses of attenuated virulence are required for active immunization against poliomyelitis. Salk vaccine belongs to the first group; it contains strains of 3 types of poliomyelitis virus inactivated with formaldehyde. Since the Salk vaccine has been used in about 100 million persons and has given protection against the paralytic form of poliomyelitis, it may seem superfluous that immunization experiments are still being carried out with avirulent poliomyelitis viruses. However, test immunizations with living viruses date back to 1950, whereas "field trials" with the Salk vaccine were not begun until 1954. Both types of immunization have their advantages and disadvantages. Simultaneous immunization against all 3 types of poliomyelitis and absence of excretion of virus are some of the advantages of the killed virus vaccine of the Salk type. Oral administration, good and prolonged immunity, and absence of allergic reactions are advantages of immunization with the living avirulent virus.

The authors felt that the advantages of immunizawith living viruses justified further vaccination experiments under clinical, virologic, and serologic control. They administered the attenuated type 1 poliomyelitis virus of H. Koprowski, known as the "Chat-Strain," by mouth to 115 persons (40 adults, 46 children, and 29 infants). The immunization produced no symptoms in any of these persons, and no case of poliomyelitis was observed during the immunization and for 3 months thereafter in the locality where the test persons resided. Poliomyelitis virus was demonstrated in the stools on the 10th day in 90% of the vaccinated infants and children and in 45% of the adults. Fifty-eight of 60 persons who had no antibodies against poliomyelitis virus, type 1, before the oral immunization showed a titer increase to 1:50 and higher. Only 2 adults showed no measurable increase in antibodies.

BOOK REVIEWS

Treatment of Cancer and Allied Diseases. Volume I: Principles of Treatment. By fifty-five authors. Edited by George T. Pack, M.D., F.A.C.S., Attending Surgeon, Memorial Center for Cancer and Allied Diseases, New York, and Irving M. Ariel, M.D., F.A.C.S., Associate Clinical Professor of Surgery and Associate Attending Surgeon, New York Medical College, Flower and Fifth Avenue Hospitals, New York. [To be in nine volumes.] Second edition. Cloth. $22.50. Pp. 646, with 505 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This is the first of nine volumes to be published. The other eight are to be concerned with specific neoplasms according to their origin in anatomic areas or systems. The first edition was in two volumes of such size as to be read only at a sturdy desk or table; the present volume is considerably smaller than the earlier books but still too heavy for armchair use or for reading in bed. Fifty-five authors have contributed to this volume alone, to accomplish a general review of organization (clinics and home care), diagnosis and pathology, some features of surgical therapy, methods of irradiation (5 of 10 section are devoted to this), hormonal treatment, chemotherapy, care of incurables, and reporting of end-results.

It is obvious that in the 37 chapters there is much important information although the overlapping, the conflicts of opinion, and the rapid obsolescence common to all such encyclopedic efforts are apparent here. Subjects which are presented in a superior fashion in the opinion of this reviewer include biopsy diagnosis, exfoliative cytology, electrosurgical treatment, radiosensitivity, the physical basis of radiation therapy, chemotherapy, and the reporting of end-results. The last-named section provides clear, practical guidance on the "why" and "how" of pertinent statistical methods. In a chapter on care of the patient before and after operation Ariel and Pack present a scholarly review of the problems in the biochemical and metabolic changes that follow the operative treatment of cancer. There is room for doubt that the practicing surgeon's basic knowledge will be enlarged significantly thereby, but the neophyte should be acquiring such information as part of his formal training.

Although there are advantages in low-voltage, short-distance (*sic*) x-ray treatment of surface lesions, the measurement of tumor dose by the "D½" or any other method is tricky, and much of the information presented in this connection is unconvincing. An important section on current palliative treatment by hormonal methods unhappily is poorly organized, frequently repetitious, and sometimes inaccurate. Written by one of the pioneers in the androgenic therapy of mammary carcinoma, this section shows a strong bias for androgens and perpetuates some of the myths which persist regarding this type of treatment. These errors include a belief that androgens given for two months after oophorectomy will hasten the regression of disease, that androgens are superior in skeletal metastasis at any age, that 30% of all patients obtain regression with androgens, and that after regression does occur the hormone employed should be discontinued. Each of these statements is inconsistent with more recent reports of various authors, and in particular with the data reported periodically during the past decade—and this year in final conclusions on 580 androgen-treated and 364 estrogen-treated patients—by the Subcommittee on Breast and Genital Cancer, Committee on Research, American Medical Association. The latter report confirms the conclusions of various investigators, since rates of regression for metastasis in bone of 24% with androgens are equaled by 27% for estrogens, while in all other situations by age, site of lesions, and time of recurrence, estrogens are either equal or superior to androgens in women four or more years postmenopausal. Other inaccuracies in this chapter are an apparent confusion of 'fibroadenoma' with dysplastic adenosis, an expression of the invalid taboo against substitutional use of estrogens for genuinely severe menopausal symptoms in women previously treated for breast cancer, a failure to emphasize the dominant role of orchiectomy in prostatic carcinoma, and a tacit approval of adrenalectomy for the latter neoplasm. Perhaps a clue to the unsatisfactory state of this section is found in the 141 references listed; divided by five-year intervals beginning in 1946, 52 of the bibliographic items were published prior to 1946, 41 and 43 in the next two five-year periods, and only 5 in 1956 or later. A single area so deficient must dampen one's admiration for the whole. The penalty for the lapse of time from manuscript to book is particularly evident in connection with methotrexate, triethylene melamine, triethylene thiophosphoramide (Thio-Tepa), nitrogen mustard, Methadone hydrochloride, and pantopon hydrochloride.

This is still a valuable reference source for libraries. The physical features of the book are beyond criticism. The index is detailed, and there are for all chapters reference lists of some length, inconveniently massed at the back of the book. Noted on page 609 is the most entertaining title since megavoltage units first made headlines (chapter 18, 12). It concerns the application of "Sugar-Hard X-Rays," but seems to give too little credit to the source, which is the first 1-Mev unit developed by Mudd at the California Institute of Technology.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

HISTAMINIC CEPHALALGIA

To the Editor:—*A 56-year-old man who has had histaminic cephalalgia for 10 years has shown only fair response to a course of histaminic desensitization with an ergotamine and caffeine preparation, aspirin, ACTH, and orally given steroids. What other treatment should be tried?*

Alexander Wallace III, M.D., Los Angeles.

Answer.—In a recent article, entitled "Histamine Cephalalgia and Its Relation to Migraine" (*Ann. Allergy* **16**:300, 1958), Unger concluded that histaminic cephalalgia is characterized by attacks of excruciating unilateral facial pain, inflammation of the eye, and rhinorrhea or blocking of the nose on that side; one of his patients was relieved by abstinence from pork, another by abstinence from milk, and a third by removal of infected teeth; migraine headache was also present in two of these three patients; histaminic cephalalgia and migraine headache are probably closely related; although histamine injections usually give good results, this does not prove that elaboration of histamine at the site of the pain causes the symptoms; and the theory that injections of histamine lead to desensitization is likewise not proved. A thorough search should be made for a focus of infection, especially dead or abscessed teeth or infected tonsils, and elimination diets, beginning with one from which milk, pork, and chocolate are rigidly excluded, should be followed for about two weeks. Then, if there is no relief, new diets should be tried, e. g., one which excludes wheat and other cereals and then one with avoidance of meat, fish, fruits, and vegetables, in succession.

GENERAL ANESTHETIC FOR A CHILD

To the Editor:—*Is there any type of general anesthetic which a pediatrician may use without risk to the patient in the performance of such minor operations as sutures of skin wounds, abscess drainage, and reduction of fractures or luxations?*

Juan Silverio, M.D., Marianao, Cuba.

Answer.—There is no type of general anesthetic that may be used without risk to the patient, no matter how minor the operative procedure is. The risk of anesthesia involved in outpatient procedures is greater than most, because patients are excited and often have quantities of undigested food in their stomachs. These two factors add such danger to the average risk of anesthesia that experienced anesthetists regard such cases as especially hazardous. Unless carefully managed, such patients struggle and resist anesthetic induction and later may aspirate vomitus and die. Such tragic accidents occur with alarming frequency throughout the United States. How then, does one treat children who require minor emergency operations? When possible, it is wise to allow an experienced anesthetist to assume the responsibility. Often a pediatrician or practitioner must act for himself, however. In such cases, he should definitely avoid the hazards involved in attempting both to anesthetize his patient and to perform the operation. There are several alternatives. At the outset, one should take time to quiet the child with a mild sedative which will calm but not depress him. Pentobarbital, or a relatively small dose (0.5 mg. per year of age) of morphine, is effective. Time must be allowed for such a drug to act. An understanding physician can accomplish a great deal by reassuring the child and gaining his confidence.

If, after this preparation, the physician uses local infiltration anesthesia, he will be able to take care of most minor lacerations and similar injuries. Ethyl chloride spray may be used if abscesses are to be opened. If a Colles' fracture is to be reduced, the fracture site may be infiltrated with a 1% solution of procaine or the fracture may be adroitly reduced without anesthesia. These measures fall short of the ideal, but they are definitely safer than would be the use of a general anesthetic by an untrained person. In many areas, a pediatrician may obtain enough training in anesthesia to justify his use of short-acting agents, such as vinyl ether, which has definite advantages for minor operations. This agent, however, may cause severe convulsions and hypoxia, or toxic liver necrosis, and consequently should not be used by trial and error methods.

ADRENOCORTICAL STEROIDS

To the Editor:—*Is there any indication for or any adequate proof of the advantage of adrenocortical extract over the various synthetic adrenal steroids (prednisone or ACTH) in the treatment of any condition? Please comment on the use of adrenocortical extract in chronic congestive heart failure, presumably refractory to routine therapy; it has been said that, in this condition, adrenocortical extract has advantages over ACTH.*

Warren F. Wilhelm, M.D., Kansas City, Mo.

Answer.—Adrenocortical extract is theoretically a composite of the steroids found in the adrenal cortex and so should have multiple effects. For practical purposes, however, it resembles desoxy-

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

corticosterone acetate in its action; that is, it is more like the mineralocorticoids than the glucocorticoids. Such synthetic adrenal steroids as prednisone and ACTH have primarily a glucocorticoid effect. Therefore, adrenocortical extract would be preferable in those situations requiring a mineralocorticoid effect, for example, in acute adrenal insufficiency, where a low serum sodium level and a low extracellular fluid volume are the immediate concerns. In regard to chronic congestive heart failure refractory to routine therapy, one must first decide whether steroids of any kind are indicated. This class of drugs has until recently been considered contraindicated in congestive heart failure because of salt and fluid retention, which may be a serious matter. In recent years, however, some apparently paradoxical effects of steroids in inducing diuresis have been observed in patients with intractable congestive heart failure. The exact mechanism of this diuresis remains to be elucidated. Various data suggest that renal tubular reabsorptive mechanisms may be involved, antidiuretic hormone activity may be inhibited, and/or aldosterone may be influenced. As long as the exact physiological explanation for the ability of steroids to cause an increase in urinary output under certain circumstances remains undetermined, it is difficult to state whether ACTH or adrenocortical extract would theoretically be more effective. Although both have been used, in most of the reported studies ACTH, cortisone, or other agents primarily glucocorticoid have been administered preponderantly. For this reason and because adrenocortical extract is extremely expensive and relatively less available, ACTH would seem preferable should one believe that the steroids are worthy of trial in severe congestive heart failure.

EXTREME LONGEVITY

To the Editor:—*A man in a nearby place claims to be 185 years old. There are no records to substantiate his statement. Is any method available to gain at least an approximate estimate of his age? Is the technique of using carbon-14 or any other test applicable in this regard, for example, a test on dental enamel? All other tissues of the body are renewed too often to supply desired information.*

Manouchehr Gueramy, M.D., Shiraz, Iran.

Answer.—No chemical or anatomic methods are available to determine an adult's age. The use of carbon-14 is not practicable, because the turnover of carbon in the body is too rapid. In other words, the test is of little value in determining the age of living substances. In addition, the accuracy of the carbon-14 test on inert objects varies up to 150 years one way or the other.

PINWORMS

To the Editor:—*A patient has had a persistent pinworm infestation. She was exposed to them by her child seven years ago. Since then, she has had many courses of treatment. Although all the accepted drugs have been used and her home technique made sure of, she still has a recurrence every 6 or 7 months after apparently being cured. The standard treatment, including mercurial ointment, enemas, a drug by mouth (piperazine tartrate, gentian violet, oxytetracycline, and other agents), and appropriate care of the hands and linen, has been used many times. She is an intelligent, extremely neat person. The children have been rechecked regularly and no worms have been noted since the first attack seven years ago. What can be done for this patient?*

M.D., New York.

Answer.—Since the children in the family have not had pinworms since their first attack and since the mother is described as an extremely neat person, the diagnosis of enterobiasis is questionable. Is she a compulsive, highly literate woman who may be upset by the problem and who keeps imagining infection? Mothers have been seen who become severely upset about pinworm infestation and describe "worms" that do not exist. The diagnosis should be checked carefully by Scotch-tape smears taken before bathing. A series of smears should be made on three consecutive mornings, and if these show negative findings she should be firmly assured that no worms are present and told to stop looking for them. There are no carriers of pinworms. This common intestinal parasite of children does not infect household pets, as is commonly suspected.

Answer.—It is probable that the continued source of reinfection is in the home and that one or more other members of the family harbor asymptomatic infections. The simplest and most logical procedure to follow in this case would be to simultaneously treat all members of the family with piperazine, using a dosage of 50 mg. per kilogram of body weight per day, but not exceeding 3 Gm. per day, for eight consecutive days. The best results have followed the administration of the total daily dose, at one time, about two hours before breakfast.

Answer.—The ubiquitous pinworm, Enterobius vermicularis, evades all sanitary barriers and invades all classes of society. It is the most common parasitic worm of civilized man. Its peculiar, brief life cycle, lasting two to six weeks (seldom three months or longer), makes infection and reinfection sure and prompt. Eggs, when ingested, hatch in the small intestine and worms occur in various stages of development from the ileum, cecum, and appendix through the colon and rectum. There is no deposition of eggs in the lumen of the host's intestine. The gravid females, when ready to oviposit, swarm into

the rectum, usually at night. They wriggle out of the anus, causing pruritus or rectal pain. The consequent rubbing and scratching of the affected parts results in crushing the worms and smearing many thousands of embryonated eggs into the perianal area. Eggs soon mature on exposure to air and become infective. Thus, fingers, underwear, night clothes, and bed sheets create a risk of continuous or interrupted reinfection with eggs which is greater for the infested person than for others. Finger transmission of eggs from anus to mouth is the principal mode of massive or cumulative infection. Some larvae, emerging in the moist surroundings of the anus, may enter the intestine by the anal route. Eggs dislodged from the host's perianal region become widely disseminated in the house. Airborne infection with dried eggs from room dust via the mouth and nose results in chronic light infections. These singular modes of infection might help to explain the peculiarities of the case presented.

Although perianal itching at the time of the emergence of gravid females from the anus is a frequent occurrence, many adults and children harboring pinworms experience little or no pruritus and, therefore, are not conscious of infection. Pinworm infection has been discovered by the Scotch-tape anal swab technique in many unsuspecting parents of already infected children. Such persons may be justifiably regarded as the carriers of infection. There are, on the other hand, others who suffer severe pruritus from even light infections with pinworms. They probably have become allergic to the worms or their products.

The following procedures are recommended for prophylaxis and treatment: 1. All members of the household should be examined or reexamined, including the husband and servants, by the Scotch-tape swab technique. The swabs should be done early in the morning, before a bath; a series of seven should be taken on alternate mornings and especially any morning after a night when itching has occurred. All those found to be infected should be treated simultaneously. 2. The patients should be cautioned to wash hands before eating and smoking. 3. They should be told to change bed sheets, underwear, nightgowns, and similar items daily. The bed sheets should not be shaken but removed gently and laundered after each use. The rugs, curtains, sofas, chairs, and table-tops should be vacuum-cleaned once a week. 4. Before retiring at night, the patient should place a liberal amount of 5% ammoniated mercury ointment on a piece of polyethylene plastic sheet and apply it to the perianal area, holding it in place with a sanitary napkin. The patient should remove and discard it the next morning in the bathroom and take a shower, thoroughly washing the perianal area with soap and water. Freshly laundered underwear should then be put on. 5. The bathtub, toilet seat, the bathroom floor, and fixtures should be wiped with 2% saponated cresol solution.

Two new and usually effective therapeutic agents are now available: Dithiazanine, a cyanine dye, is supplied in the form of 0.1 Gm. tablets, and the adult dosage is 200 mg. (two tablets) three times daily for five consecutive days (Schwartzwelder and others, *J. A. M. A.* **165**:2063-2067 [Dec. 21] 1957). Pyrvinium chloride, also a cyanine dye, marketed as a strawberry-flavored suspension, is given in a dosage of 2 mg. per kilogram of body weight per day, in two equal doses daily for six consecutive days (*Am. J. Trop. Med. & Hyg.* **7**:212, 1958).

RECURRENT PHLEBITIS

To the Editor:—*Over the past five years, a married woman has suffered at intervals of months or years from attacks of phlebitis involving her legs from ankle to groin (three times on the right and twice on the left). Once she suffered a pulmonary embolus. On two occasions she was in Seattle, Wash., once in Long Beach, Calif., and twice here in Mexico, and everywhere physicians have been at a loss as to the cause. Treatment has included rest, hot packs, antibiotics, and anticoagulants. Attacks have lasted one to eight weeks. Please suggest a course of treatment.*

Richard H. Lyon, M.D., Jalisco, Mexico.

Answer.—This patient seems to be suffering from recurring infectious thrombophlebitis with lymphedema. The original cause is not known, but such patients are likely to develop recurring episodes with chills and fever, precipitated by mild trauma or any systemic infection, however mild. This is particularly true with recurring upper respiratory infections. In addition to rest in bed, continuous warm wet compresses over the limb, elevation of the foot of the bed, antibiotics, and anticoagulants, methacholine chloride, administered by iontophoresis every other day for a series of 10 treatments, and use of an oscillating bed are often helpful. These measures should improve the venous circulation and help overcome spasm of both the veins and arteries. Vasodilators are usually prescribed, such as nylidrin (6 mg. given three times a day before meals) and papaverine hydrochloride (60 mg. given after meals and at bedtime). In chronic cases, when there is evidence of an active perivenous inflammation, trypsin therapy (2.5 mg. given twice daily for 10 days) is helpful. The condition usually is reasonably controlled in two or three weeks. The important thing is to continue the treatment for a prolonged or indefinite period. The patient should wear an elastic support for at least three months. Anticoagulant therapy should be continued for at least six months but should be properly supervised with prothrombin time estima-

tions. Another suggestion which may be applicable here would be to continue the antibiotic therapy, particularly if the source of infection is determined. Sometimes it may be in the sinuses, throat, or urinary tract. In such cases 200,000 units of penicillin and 500 mg. of a triple sulfonamide, such as sulfadiazine, sulfamerazine, and sulfamethazine, may be given daily for a prolonged period. This measure may be helpful in preventing recurrences.

Reference

Kramer, D. W., and de Medeiros, A.: Medical Management of Thrombophlebitis and Postphlebitic Syndrome: Survey of 400 Treated Cases from Series of 779 Consecutive Cases of Phlebitis, J. A. M. A. **165**:767-773 (Oct. 19) 1957.

PAIN IN LOWER EXTREMITY

To the Editor:—*A man, aged 47, who works actively every day complains of pain in the left lower extremity. It began suddenly seven years ago while he was walking down a steep hill. The pain in his left hip, thigh, and calf at that time was so severe he could not bear weight on the left side. He spent the next hour or so working himself up to the point of being able to walk again after sliding down the hill the rest of the way and walking to the car. Then he recovered completely, but ever since then, whenever he walks 100 yards quickly, a sudden pain in the thigh and calf stops him "dead" and he has to take the weight off the left lower extremity and rotate it inward and outward at the hip, which relieves it within five minutes. Then he is perfectly all right, with no residuals. He has tried sitting down when the pain strikes him, but that does not help. If he is walking more slowly the pain comes gradually but is treated the same way, and if he walks slowly enough he can walk all day without pain. At worst the calf will cramp; otherwise, there is a deep-seated pain in the whole thigh and leg which he cannot localize because there is no tenderness. A few times the foot has tingled slightly. There is no subjective skin temperature or skin color change. Pulsations in the dorsalis pedis artery are good. There is never any swelling or trophic change. Five or six physicians, including a specialist, have examined him. Please suggest treatment.*

Robert S. Hamilton, M.D., Conrad, Mont.

Answer.—From the history, it is presumed that the circulatory function studies have given normal results. It is possible that this patient may have arteriospasm with a claudication-like pain at times. He may have some marked irritation of the posterior nerve roots. This may have been a sacroiliac condition at the onset or, more likely, a disk syndrome. Walking down the hill may have set off some pathological changes of the ligaments around the spine, which permitted some injury to the spine or slipping of an intervertebral disk. It is also possible that the disk may slip in and out at times and may produce marked symptoms alternating with times when patient is symptom-free. This patient should be thoroughly x-rayed in reference to some spinal injury with either a neurosurgeon or an orthopedist supervising the studies. A myelogram may throw some light on this case and would enable any pathological findings to be corrected. In the meantime, the patient should be treated with analgesics and vasodilators to overcome the arteriospasm. Further investigation should be carried out to arrive at the source and attempts made to correct the offending factor.

CHLOROTHIAZIDE AND OLIGOHYDRAMNIOS

To the Editor:—*An 18-year-old primigravida was recently delivered at term of a girl weighing 6 lb. 2 oz. (2,800 Gm.) and showing bilateral marked talipes varus but no obvious bony abnormalities. Oligohydramnios seemed to be present. During the last six weeks of pregnancy the patient was almost continuously on therapy with chlorothiazide because of excessive weight gain (25 lb. [11.3 kg.] in four weeks) and pitting edema, with a rise in blood pressure from 120/70 to 160/90 mm. Hg in the same four weeks. No albuminuria was found. With use of this drug, the patient lost 14 lb. (6.4 kg.). What is the influence of chlorothiazide on amniotic fluid, since the oligohydramnios appears to be a causal factor in the development of the clubfeet?*

M.D., Virginia.

Answer.—A number of drugs having carbonic anhydrase inhibitory activity have been used in an effort to effect a reversal of the sodium and water retention characteristic of the late toxemias of pregnancy. Of these drugs, chlorothiazide seems to be one of the most effective. The effectiveness of this type of therapy will be apparent clinically by a rapid weight loss, a diminution in edema, and occasionally a reduction in the tone and size of the uterus. The latter is especially apparent when polyhydramnios has been present. Frequent circumferential measurements will provide the best evidence of a diminishing volume of amniotic fluid. The relationship between oligohydramnios and the presence of skeletal or muscular abnormalities in the fetus, such as talipes varus, is obscure. Skeletal and muscular defects occur frequently in an abdominal pregnancy where there may be no amniotic fluid protection. On the other hand, many similar defects have been observed in premature infants and aborted fetuses when no constriction or abnormal pressure factors seemed to be present. It would seem most unlikely that the bilateral talipes

varus present in the infant described was the result of the use of chlorothiazide. Although this possibility cannot be absolutely excluded, it should be borne in mind that the hazards incident to the inadequate treatment of preeclampsia may be exceedingly great. Certainly, the active treatment of preeclampsia should be the primary objective.

COAGULATION TEST

To the Editor:—*Years ago a blood clotting test, known as the coagulation valence, was described by Fonio. The basis of the test is the ability of blood to clot when mixed with a substance which inhibits coagulation, in this case magnesium sulfate. What is the anticoagulant mechanism of magnesium sulfate, which is evident even with low dilutions of this salt? What clotting factor or factors in the blood is removed by it?* *J. H. Rogers, M.D., Gadsden, Ala.*

Answer.—Magnesium sulfate, as well as other salts of magnesium, depresses coagulation. High concentrations of calcium salts and even sodium chloride also effect an inhibitory action of coagulation. It is likely that this is a nonspecific effect and probably is not specific for magnesium. This consultant is unaware of any recent work that has been done to determine in what phase of the clotting mechanism these inorganic salts act. The older literature is noninformative, because the various clotting factors were not differentiated until recently.

Answer.—Although much work has been done on the relationship of certain cations, particularly calcium and other alkaline earth elements, to the coagulation mechanism, there is still much ignorance regarding the precise clotting factors on which they act. Interest in this area has recently been reawakened in the light of our newer knowledge of the coagulation sequence. The following information regarding the mechanism by which magnesium sulfate may act as an anticoagulant is largely derived from early work of Stefanini and Quick (*Am. J. Physiol.* **152**:389, 1948), who made studies on blood decalcified by an ion exchange resin (Amberlite). It was demonstrated that calcium is both a procoagulant as well as an anticoagulant, depending on the concentration used when re-added to the decalcified plasma. This has been recently reconfirmed with highly purified materials, demonstrating the quantitative relationships required for the biological activation of highly purified prothrombin (Goldstein, Izak, and Zonderman, *Fed. Proc.* **16**:48, 1957; Alexander, in Transactions of the Fourth International Congress of Biochemistry, New York, Pergamon Press, 1958, to be published).

DYSPNEA AND ABDOMINAL DISTENTION

To the Editor:—*A 76-year-old woman performed such heavy work as pitching hay until two years ago. Her only complaint was dyspnea easily relieved by stopping work for a few minutes. About 10 years ago a 25-lb. growth (probably an ovarian cyst) was removed from her abdomen through a midline incision. She has had a "big stomach" ever since. All other findings are normal, except for a marked meteorism; her abdominal walls are felt to be under great pressure. This condition has been present since her operation. Palpation is unsatisfactory, but there is no indication of mass or free fluid. Although she has dyspnea, she can touch the floor easily when bending over with her knees straight. What might cause such a condition? Would it be safe to give a trial dose of neostigmine?* *M.D., New York.*

Answer.—The meteorism which was noted by the examining physician might well contribute to this patient's dyspnea, but one would have to attribute it mostly to the arteriosclerotic heart disease which must be present. The enlargement of the abdomen may be due to many causes, but the three most obvious, in view of the patient's history, are recurrent tumor, ascites, or intestinal distention. In view of the time since her operation and the absence of masses or free fluid, the sole cause must be a distended colon. The colon is probably dilated, secondary to a functional or organic partial obstruction in the lower sigmoid or rectosigmoid. A functional obstruction may be due to degeneration of the myenteric plexus caused by nutritional deficiency. Partial organic obstruction could be produced by diverticulitis, operative adhesions, or a chronic twisting or kinking as the sigmoid enters the pelvis. The diagnosis will depend on sigmoidoscopy, roentgenograms of the abdomen, and a barium enema. If these studies demonstrate a functional obstruction (acquired megacolon) it may be controlled by enemas and saline solution laxatives. The various choline derivatives have not proved satisfactory in such older patients because of their cardiovascular side-effects.

CARBON MONOXIDE AND CORONARY INFARCTION

To the Editor:—*Could a few whiffs of fumes from an automobile exhaust precipitate a coronary infarction? A 65-year-old man inhaled such fumes and within 15 minutes developed an acute coronary occlusion.* *M.D., Illinois.*

Answer.—The question implies a very brief exposure to automobile exhaust gas, and it can be assumed that this exposure was not followed by any long period of unconsciousness due to deprivation of oxygen. It is highly improbable that there could be any connection between the exposure described

and the appearance of the coronary accident. Automobile exhaust gas does have other components than carbon monoxide, usually small amounts of hydrocarbons, but the effect of these contaminants on the general toxicity of the exhaust gas is negligible. Exposure to carbon monoxide results in the reduction of the available oxygen in the respired air. Symptoms are primarily due to oxygen deprivation, depending on the concentration of the carbon monoxide in the air and the duration of the exposure. The effect may be entirely negligible or, when severe, will manifest itself chiefly by injury to the nervous system, which characteristically shows the effect of oxygen deprivation to the tissues. Any effect on the circulatory system would be secondary and the result of a serious exposure to carbon monoxide, which would have resulted in a prolonged period of unconsciousness. Many observers, reporting in the past, attributed various changes noted in the blood vessels and heart to carbon monoxide exposures, but little evidence has ever been presented to justify these claims. The exposures assumed to have produced vascular effects were extreme. The vascular changes attributed to carbon monoxide exposure could not have occurred in the brief time mentioned, in which the appearance of a coronary occlusion was within a few minutes after exposure to the exhaust fumes.

POSTOPERATIVE PULMONARY EMBOLISM

To the Editor:—*Does general anesthesia contribute to fatal postoperative pulmonary embolism? This tragic complication continues to occur in spite of good operative and postoperative care, including such measures as maintenance of blood pressure during operation, elevation and massage of the lower limbs, elimination of pressure on the lower extremities, and early ambulation. Is the incidence of fatal postoperative pulmonary embolism greater after general anesthesia than after spinal anesthesia?*

F. A. Procunier, M.D.
Waterford, Ontario, Canada.

Answer.—This consultant does not believe that general anesthesia contributes in any way to nonfatal or fatal postoperative pulmonary embolism. With few exceptions, pulmonary embolism is a result of a bland thrombus in the vein, one which is not associated with phlebitis, and, therefore, the clot is not firmly attached and can become detached. This has been called phlebothrombosis in contradistinction to thrombophlebitis. Phlebothrombosis is probably due to two predisposing factors. One is an increased tendency of the blood to clot, resulting from tissue injury. It apparently does not make much difference whether the cause of the tissue injury is operative trauma, accidental trauma, or invasion of tissue by neoplastic disease or infection. Whenever there is tissue injury, there is an increased tendency of the blood to clot. The other predisposing factor is circulatory retardation, and it is for this reason that most phlebothromboses occur in the lower extremity, because of lack of movement of these extremities in a patient who is in bed. The incidence of pulmonary embolism apparently is no higher in patients operated on under general anesthesia than in those operated on under spinal anesthesia.

DIVERTICULITIS

To the Editor:—*An 82-year-old woman who had been in good health suddenly developed intestinal obstruction due to an inflammatory diverticulum in the sigmoid colon. A cecostomy was performed to relieve obstructive symptoms. The patient's condition returned to normal except for a profuse watery fecal discharge through the fistula, requiring four heavy dressings daily. At the time of writing, three months after onset, there has been no normal bowel movement. Should a colostomy be performed and the fistula closed?*

C. C. Dillon, M.D., Sidell, Ill.

Answer.—Since the patient's condition has returned essentially to normal, surgical exploration in the hope of resecting the segment of diverticulitis would be in order. If this cannot be done, a colostomy might be established in the descending colon and proximal to the diverticulitis. In due time, and possibly several months after resection or after colostomy, the cecostomy could be closed. This should make the patient much more comfortable.

PROTEINURIA

To the Editor:—*What is the significance of a finding of 2+ or more albumin in the urine with or without 5 to 10 red blood cells or 5 to 10 leukocytes? In review of hospital records, this has been a common finding in patients who are hospitalized for conditions other than genitourinary disease. Does this show a lowering of kidney reserve, or is it just a manifestation of a generalized toxic condition? A woman who is menstruating has 4+ albumin in the urine with gross blood. Can this finding be attributed entirely to menstruation? A patient who comes in for an operation, such as a herniorrhaphy or dental extraction, may show 2+ albumin with 10 red blood cells and 10 leukocytes in the urine. Is this significant of genitourinary pathology? A point of discussion is that these findings are to be ignored if they are not based on catheterized specimens.*

Nerico W. Pioppi, M.D., Southbridge, Mass.

Answer.—The finding of 2+ albumin in the urine in the presence of a generalized toxic condition is of no particular significance, but, in an otherwise healthy patient with only a few white or red blood cells in the urine, such a finding should be care-

fully investigated. In the menstruating woman, the finding of a high degree of albuminuria can be entirely normal. The best way to determine this is to wait until the menstrual period is over and recheck one or two more specimens. It is true that, with the highly sensitive tests so commonly used today, the presence of a trace or up to 1+ albuminuria may be within normal limits. This consultant does not believe that it is always necessary to have a catheterized specimen of urine to appreciate the importance of albuminuria, but it is impossible to make any suggestions concerning cellular findings in the urine specimen from a woman unless it is a catheterized specimen.

GASES IN NEON LIGHTS

To the Editor:—*What gases are used in neon lights? Are they injurious to persons working with them?*

W. J. Tucker, M.D., Ashland, Wis.

Answer.—The gases likely to appear in the neon type of light, but not all in any one style or form, are neon, krypton, argon, xenon, and helium. All of these gases are essentially harmless, acting only as simple asphyxiants. Any damage connected with the manufacture of these light tubes is more likely to be identifiable with the phosphors contained rather than the gases. Although all beryllium is believed to have disappeared from ordinary fluorescent lighting tubes, it may be suspected that some beryllium may be surreptitiously introduced into some of the neon type of tubes. If this is true, this practice is more likely to exist in small rather than large manufacturing plants.

RESTORATION OF DIVIDED VAS DEFERENS

To the Editor:—*A 30-year-old man stated that at the age of 27 he had a partial vasectomy, which apparently failed in that the sperm count remained high. One testis had previously been removed, apparently because of a severe injury. The second time the vasectomy was performed, an inguinal incision was made and, presumably, a segment of the vas deferens was removed. The patient said his physician told him the vas was removed "down next to the prostate." The patient has two children by a former marriage, and now he is anxious that his present wife become pregnant. The problem seems to resolve itself into two approaches: (1) reanastomosis of the divided vas deferens and (2) aspiration of spermatozoa from the epididymis. Please offer suggestions as to the details of aspirating spermatozoa for cervical injection and give references for surgical restoration of the divided vas deferens.* *M.D., Illinois.*

Answer.—Reanastomosis of the divided vas deferens has proved successful to a varying degree. In recent years several reports (O'Conor, *J. A. M. A.* **136**:162-163 [Jan. 17] 1948; Dorsey, *J. Internat. Coll. Surgeons* **27**:453, 1957) have been made of a series of such operations which have proved to be successful in many cases. If reanastomosis is attempted, it should be done by a urologist who has had wide experience with this operation. Aspiration of spermatozoa from the epididymis has not been successful in many cases. In the first place, it is difficult to collect a sufficient number of spermatozoa by aspiration to achieve insemination. Furthermore, the spermatozoa would not have opportunity to mature without having passed through the epididymis and vas. The possibility of collecting a sufficient number of spermatozoa by means of an operation causing dilatation of the vas has been suggested.

DISINFECTION OF FLOORS

To the Editor:—*What germicide is best suited for cleaning floors that might be contaminated with Mycobacterium tuberculosis? Is any antiseptic more effective than phenol?*

Denvil F. Crowe, M.D., Paris, Tenn.

Answer.—Washing the floors and woodwork of rooms contaminated by tubercle bacilli with soap and hot water and subsequent wetting with a 2 to 5% solution of *o*-phenyl and methyl phenols remains the standard recommendation. Among the newer compounds, a 2.5% solution of *o*-phenyl and *p-tert*-amyl phenols with potassium ricinoleate is highly recommended; it has the advantage of being odorless.

REPEATED CONGENITAL DEFECTS

To the Editor:—*One year ago, a 22-year-old woman delivered a female infant who died shortly after birth due to bilateral cystic kidneys, hydrocephalus, porencephalic cyst, intra-atrial septal defect, and tricuspid valve atresia. Recently, she delivered a second female infant who died shortly after birth due to bilateral cystic kidneys, hydrocephalus, and encephalocele. She has had no other pregnancies. Neither the husband nor the wife has any congenital defects, and there is no history of such defects in their families. What advice should be given to this couple regarding a future pregnancy? Should husband and wife be investigated for congenital kidney defects? Would semen examination be of any value?*

Edward B. O'Connell, M.D., New Haven, Conn.

Answer.—The abnormalities of these infants could be due to a combination of hereditary defects and "errors of development." It is impossible to determine which is the more important in each individual abnormality. Hydrocephalus is often inherited as a recessive characteristic. If it is inherited in this instance, both parents had the tendency, which was not, however, expressed in them. The statistical expectation would be that one

child out of every four would be hydrocephalic. Since the mother has already borne two affected children, there would be a good chance that the next one would be free from this defect, but the other serious defects might be present. In view of the number and seriousness of these, the prognosis is so doubtful that the couple might well be advised not to risk another pregnancy. Semen examination would be of no value.

HYPOGLYCEMIA

To the Editor:—*Is there any truth to the theory that a low blood sugar level (cause unknown) may be made worse by the administration of dextrose or the frequent use of glucose (hard candy) given orally? The supposed theory is that the dextrose will activate the pancreas to produce more insulin and thus further reduce the blood sugar level. A patient had a blood sugar level of 52 mg. % and weak spells. Exploration was done, and no tumor could be found in his pancreas. He now says he gets along better if he uses no sugar and thinks his blood sugar level is up to 105 mg. %. Is this likely?*

George C. Christie, M.D., Canon City, Colo.

Answer.—As far as an immediate effect is concerned, the administration of dextrose tends to elevate the blood sugar level, but as a long-term effect in persons with so-called functional neurogenic hypoglycemia a high carbohydrate intake usually aggravates the condition. This comes about presumably because of an overly great response of insulin-producing cells to the stimulus of a rising blood sugar level. In such persons the blood sugar level after an overnight fast is normal but may fall to hypoglycemic levels two or three hours after eating. Treatment consists of (1) a diet low in carbohydrate, liberal in protein, and with enough fat to provide adequate calories; (2) between-meal snacks which are low in carbohydrate; (3) small doses of phenobarbital and belladonna; and (4) relief from tension and stressful situations. Assuming that the patient in question does not have an islet cell tumor, these measures may prove beneficial. The article by Conn and Seltzer (*Am. J. Med.* **19**:460, 1955) should be consulted.

POSTERIOR PITUITARY INJECTION AND GENERAL ANESTHESIA

To the Editor:—*Is the use of posterior pituitary injection as a local vasoconstrictor in surgery contraindicated when general anesthesia is used?*

M.D., New York.

Answer.—In anesthesia produced by agents having a direct action on the heart and, under some conditions, all commonly used general anesthetic agents are cardiac depressants, posterior pituitary injection should be avoided as a vasoconstrictor. This is due to the fact that this drug contains vasopressin tannate, which has a constricting action on the coronary arteries, and, when this is combined with myocardial depression, pronounced hypotension may result. Myocardial and coronary artery disease must also be considered as contraindications to the use of this drug. If this agent is slowly absorbed, there is little likelihood of a severe reaction, but as long as there is a possibility of accidental intravascular injection one must be prepared to accept the results of coronary constriction. If the patient is predisposed to asthma or if cyclopropane is being used, laryngospasm, bronchospasm, or bronchorrhea may also result from posterior pituitary injection.

Reference

Parsloe, C. P.; Morris, L. E.; and Orth, O. S.: Relationship of Various Anesthetic Agents to Action of Pituitrin, Pitressin, and Pitocin, Anesthesiology **11**:76-93 (Jan.) 1950.

TESTICULAR TUMORS

To the Editor:—*Is there any evidence that testicular tumors occur with any greater frequency in men who have had vasectomies?*

Joe J. Horn, M.D., Plainview, Texas.

Answer.—Vasectomy has no effect on the testis other than obstruction to the passage of its spermatozoa. Spermatogenesis and formation of Leydig's cells continue undisturbed. A review of the literature has disclosed no increased incidence of tumor formation of the testis after vasectomy. Occasionally, spermatozoa are found invading the tissue of the epididymis, producing a tumor-like swelling which is actually granulamatous. Such granulomas are not necessarily associated with vasal or epididymal obstruction.

COUGHING AFTER CATARACT OPERATION

To the Editor:—*A 60-year-old man has cataracts of both eyes. The vision of the right eye is 0 and of the left 20/250. The patient also has hypoparathyroidism, which is controlled, and more important, bronchiectasis of both lower lobes which causes frequent coughing. Is it possible to stop coughing during and for a few days after the cataract operation? Is it possible to keep the intraocular pressure steady after the cataract operation? The tension of the eyes is normal.*

Arnold Ernest Aszody, M.D., Corona, N.Y.

Answer.—With the present-day technique of cataract extraction and with the use of corneoscleral suturing of the incision, a patient who coughs during or after such an operation is no longer considered with the fear that was formerly held. An evaluation of the bronchiectasis should be made prior to cataract extraction. After this, the management of the pulmonary condition should be undertaken to clear up any infection. Both before and after operation, small doses of codeine or similar drugs may be used to suppress but not abolish the

cough. The intraocular pressure can be maintained postoperatively by an adequate iridectomy at the time of operation, the use of miotics locally, and the oral use of any of the effective, long-acting inhibitors of cholinesterase, such as acetazolamide, chlorothiazide, and ethoxzolamide. None of these drugs should be used without the proper indication, namely, increased intraocular pressure.

GAMMA GLOBULIN DEFICIENCY

To the Editor:—*Two small boys have an extreme gamma globulin deficiency. The father's employment requires long periods outside the United States. Since these children probably cannot develop active immunization, is there any value in giving them anti-diphtheria-pertussis-tetanus (DPT) injections and would it not be dangerous to vaccinate them against smallpox? Would these children not have as much protection with their regular gamma globulin injections as if they were receiving active immunizations?*

Spencer C. Manrodt, M.D., Melbourne, Fla.

Answer.—It would be hazardous indeed to vaccinate these boys against smallpox. The risk of giving them DPT injections would far outweigh the possible good obtained. For maximum protection it would be safer and preferable to administer intramuscularly or subcutaneously (not intravenously) the proper dosage of pooled adult gamma globulin once every four to six weeks. The dose is computed by body weight. Infectious hepatitis, measles, poliomyelitis, and possibly other diseases should be prevented or ameliorated by 5 to 10 ml. of potent gamma globulin per 100 lb. of body weight. The antibody content of 1 ml. of gamma globulin should be the equivalent of 25 ml. of whole serum. Its use is accompanied by less discomfort and no reactions or hazards, if syringe and needle are properly sterilized and the site of injection properly cleansed with 70% alcohol and a sterile pledget of gauze or cotton. Gamma globulin deficiency can be managed by the administration of 0.1 ml. per kilogram of body weight monthly.

SMOKE POISONING

To the Editor:—*Are there lethal factors beyond carbon monoxide, heat, and asphyxia inherent in the smoke poisoning encountered in a burning building?*

I. G. Frohman, M.D., Rockaway Beach, N. Y.

Answer.—Depending on the combustible content of the building, the possibilities are legion. Among others are nitrogen dioxide leading to pulmonary edema, irritant aldehydes conducive to pneumonitis, and hydrogen cyanide from the partial combustion of such objects as wool rugs or wool upholstery. Sulfur dioxide is always present and might reach lethal concentration. Partial combustion may lead to the presence of hydrogen sulfide. Carbon dioxide may be active over and above its simple asphyxiant properties. Depending on the nature of the fire-fighting equipment, phosgene may arise from the decomposition of carbon tetrachloride. Particulate matter, such as carbon, contributing to the smoke may enhance the activity of some of the chemicals mentioned. This list could be expanded extensively. Many of the larger fire insurance companies publish lists of the major constituents of poisonous smokes.

TORTICOLLIS

To the Editor:—*Is there any satisfactory treatment for chronic wryneck? In a 48-year-old woman who is going through the menopause and whose general health is reasonably good, this condition has come on in the past few years. She now holds her head constantly on the left and at times she pushes it back to the normal position with her left hand. She was told to take meprobamate and found it of some aid. The general examination is negative except for moderate scoliosis in the cervicothoracic spine.*

Alan R. Anderson, M.D., Freeport, N. Y.

Answer.—Spasmodic torticollis is one of the movement disorders for which there is no satisfactory treatment. Tranquilizers, such as meprobamate, occasionally give slight relief, and some of the anti-Parkinsonian remedies may be of slight benefit; however, for the most part, drugs have little effect. Neurosurgical intervention is occasionally recommended but may provide no real improvement. This has consisted in removing a portion of the hypertrophied sternocleidomastoid muscle and section of various of the upper cervical roots. More recently, destructive lesions of the basal ganglions have been tried. These patients sometimes are helped by psychiatric counseling when there is evidence of marked emotional instability.

"TRI-OPTIC LENS"

To the Editor:—*An article in* Newsweek Magazine *(Oct. 27, 1958) stated that there is a tri-optic plastic lens that will give good vision. Is such a lens available on the market? Where can it be purchased?*

Odell J. Kirksey, M.D., Mulberry, Ark.

Answer.—Experience at several centers has shown that, generally, near-blind persons find more useful a particular lens for whatever their specific visual requirement may be than the complicated lens described. A high-power, relatively inexpensive lens fitted in a spectacle frame can be used for reading. The best correction can be used for ordinary travel. These two corrections can be combined in a bifocal lens, if such is desired. If a nearly blind person wishes to see something like a street sign, he can use a pocket telescope such as the "penscope," available through the American

Foundation for the Blind, 15 W. 16th St., New York 11. For sports events, some patients like to use low-power binoculars. Before any special lenses are fitted, a person should have a thorough ophthalmological examination. Apparently the "tri-optic lens" is available only through its inventor.

CAUSE OF OLD INFARCT

To the Editor:—*A man, aged 29, has an old healed infarct of the anterior coronary branch without any significant history other than that he was temporarily paralyzed at the age of 9 by a bolt of lightning. Clinically, he is quite well. Could this accident have damaged the vessel?*

Malcolm L. Raymond, M.D., Johnstown, Pa.

Answer.—A generalized electric shock should not have a selective effect on a coronary branch. At the age of 9 years, atherosclerotic damage is not likely. It is possible to have a relatively painless infarction of a coronary branch. The patient's pain threshold would be a factor.

TREATMENT OF HEPATITIS

To the Editor:—*In a recent issue of a German medical publication,* Drug Research, *an article appeared on the treatment of different forms of hepatitis by means of a substrate consisting of supravital liver cells coupled to a bacterial haptene. Please comment on this type of therapy.*

Emily A. Svoboda, M.D., Chicago.

Answer.—The variable and unpredictable course of any given case of hepatitis has led to claims for many forms of therapy which further experience has shown to have been unfounded. The use of "supravital liver cells coupled to a bacterial haptene" has no rational basis, nor is there any convincing evidence of its efficacy. For the present, reliance on generally accepted symptomatic and supportive measures for the treatment of hepatitis is indicated.

NUTRITION FOR A PATIENT WITH TWENTY CENTIMETERS OF JEJUNUM

To the Editor.—*An additional therapeutic measure to those that were offered in the Questions and Answers column on the subject of nutrition for a patient with 20 cm. of jejunum* (J. A. M. A. **169:**201 *[Jan. 10] 1959) is the use of corticosteroids. We have given prednisone (and before that cortisone) with much success to patients with jejunoileitis who have undergone massive resection. The usefulness of corticosteroids lies in their ability to increase the absorption of fluids, electrolytes, and nutrients from the intestines. The dose may vary from 15 to 30 mg. of prednisone per day. This should be fortified at monthly intervals by ACTH and, in this case, by a male hormone. Despite the colostomy, the administration of steroids should be rewarding. The use of the term regional ileitis for such extensive disease requires some elaboration. Ileocolitis, regional enteritis, and nonspecific jejunoileitis are more precise terms.*

A. I. Friedman, M.D.
405 State St.
Hackensack, N. J.

SMALLPOX VACCINATION

To the Editor:—*An item in Questions and Answers* (J. A. M. A. **169:***198 [Jan. 10] 1959) stated that failures to develop a primary take of smallpox vaccination were due to faulty vaccination technique or to the use of vaccines which had lost their potency because of improper or prolonged storage. A woman has had repeated vaccinations for smallpox without a take. Vaccinations have been performed by a number of physicians, including myself, with vaccines that had proved effective in other patients. A son, aged 2½ years, also has had repeated vaccinations without a take. A daughter, aged 10 months, has had a successful take. I am wondering if others have had similar experiences and if other factors in the take of smallpox vaccination are to be considered.*

Horace A. Deford, M.D.
34th Air Division (Defense)
Kirtland Air Force Base, N. Mex.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Experimentally it has been shown that the state of nutrition and hormone balance of an animal affects the growth of vaccine virus and the lesions it induces (*Smadel, in Viral and Rickettsial Diseases of Man, *edited by Thomas E. Rivers, Philadelphia, J. B. Lippincott Company, 1952). In man it may be that due to these or other factors some persons are truly resistant—at least temporarily—to smallpox vaccine. There is, however, evidence that such persons are rare and, for the most part, repeated failures to take are due to a faulty technique or to the use of an inactivated vaccine. The fact that a particular lot has proved successful in other patients does not necessarily mean that it should also be successful in a particular individual. As stated by Leake (*Questions and Answers on Smallpox and Vaccination, Public Health Report, *reprint 1137), "differences in skin receptivity may occur independently of the condition of the individual as regards true immunity. . . . Some individuals may be resistant . . . to a lot of vaccine which gives success generally in other individuals, but are not immuned against smallpox when exposed, nor against vaccination when a fully potent lot of vaccine is used."*